HUMAN DIVERSITY

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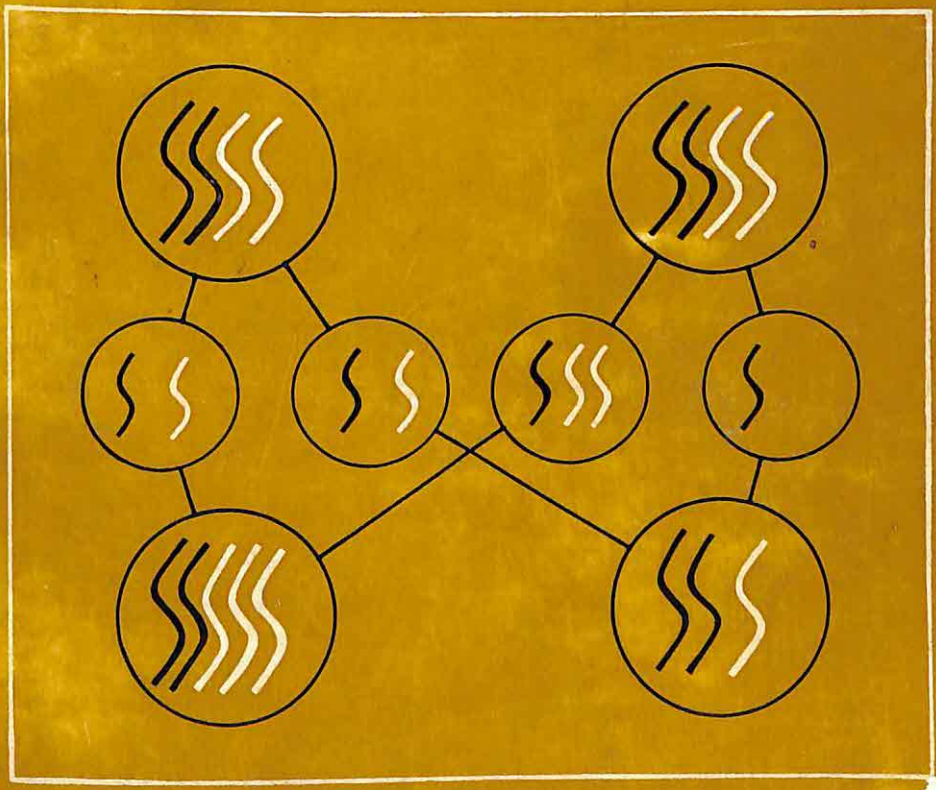

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THE NATURE AND SIGNIFICANCE OF DIFFERENCES AMONG MEN

KENNETH MATHER
C.B.E., D.Sc., F.R.S.

Vice-Chancellor
University of Southampton
formerly
Professor of Genetics in the
University of Birmingham

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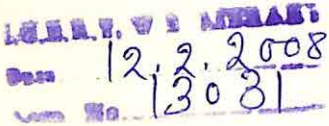

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Preface

This book is based on the Ballard-Matthews Lectures which I was privileged to give in the University College of North Wales in 1960. It is not directed towards the professional biologist, though I hope that at least a few biologists will find interest in it. Rather I have set myself the more ambitious task of presenting my subject to a wider public—in fact to all who are seeking a better understanding of human differences and their importance for our populations and societies.

Each of us is unique, and our diversity affects everything that we do. In its turn it is prospectively affected by everything that we do, as individuals and especially as a society. Society is built on differences. Some of these differences we are apt to pretend do not exist. Others we recognise and seek to accommodate in our social structure. And in seeking to accommodate them we are liable to alter their incidence as well as their impact, for we do not always recognise their true causes and so necessarily fail to see the consequences of the actions that we are led to take. Not that I, or indeed anyone, can at present see far below the surface except perhaps in a few special cases. True, we are beginning to learn at least something of the complexity of diversity, its causation and its significance; but it is a matter of which we must know very much more if we are to understand ourselves, our societies and our destiny. To do so will demand a great deal of work by a great many people of diverse interests and approaches. Yet vital though it is, the effort will not be made unless sufficient of us appreciate the need for it. If this book contributes to that appreciation I shall be well rewarded.

I have necessarily presented the picture as I see it, from the point of view of a geneticist, though I hope without underestimating the importance of aspects other than the genetical.

I have not set out to present an account of genetical principles—nowadays such accounts exist in plenty at all levels of sophistication and detail—but I have introduced such of them as are necessary, in what I trust will be an intelligible way. In a few places I have also ventured to use a little mathematics. This need not put the reader off: none of it goes beyond the "O" level; and it can be skipped, though I hope it will not be because even the most elementary mathematics can lend to an argument precision and clarity achievable in no other way. I believe too that many of us are frightened by it to a quite unnecessary degree: basic mathematics is much easier to learn and use than is basic English or basic French.

I am indebted to all those of my colleagues, particularly in the University of Birmingham, who have encouraged me to write this book. I hope they are not disappointed by the outcome. I am especially grateful to Professor R. Pascal, Professor T. J. B. Spencer and Dr J. A. Fraser Roberts, F.R.S., all of whom have most kindly read and commented on the manuscript. It is a pleasure also to acknowledge the help Dr Fraser Roberts and Professor T. McKeown have given me by supplying information that I needed on certain points.

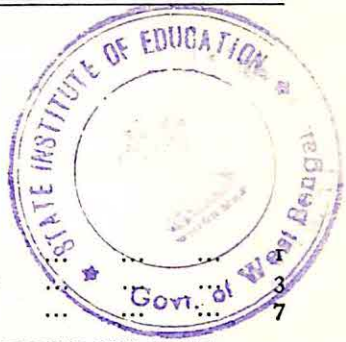
KENNETH MATHER

Birmingham, 1964

It is a great pleasure to me that a reprint of *Human Diversity* has been required, for it encourages me to believe that I have, at least in some measure, achieved my aim of interesting a wider public in the search for understanding of human differences and their significance. I trust that the book's reissue in a paperback form will serve to introduce it to still further circles of readers.

KENNETH MATHER

Southampton, 1966



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The Study of Diversity

Diversity is a commonplace of life. Biologists distinguish over a million different forms, or as they would say species, of living creatures, and even the least biologically minded city dweller would recognise at sight some scores of different kinds of plants and animals. Nor is this more than a beginning, for the deeper our interest in a species and the better we learn to know it the greater the diversity we come to see among the individual animals or plants of which it is made up. All of us are familiar with the variety to be seen among say cats and dogs—a variety not merely of size, shape, colour and pattern, but of temperament and behaviour too; and we have little difficulty in recognising our own dogs and cats as individuals whose features and ways set them apart from the rest of their kind. The diversity we recognise is limited only by our interest and understanding, so that when we come to the most familiar species of all, the one in which our interest is necessarily greatest, man himself, we accept as a matter of course that no two individuals are alike. Indeed the very organisation of human society and even the trivia of daily life assume that each of us is distinguishable at once from his fellows. We take for granted that human diversity is complete and indeed the confusions that can arise when differences are small have provided the plots for stories since time immemorial. The favourite such confusion, the one round which Shakespeare built *A Comedy of Errors*, is that between identical twins. Identical twins can indeed be confusing to the chance acquaintance but even they are always distinguishable to their parents and others who know them well. Their differences may be small but they always exist: discrimination may require intimate knowledge, but it is always possible.

We rely chiefly on visual means for identifying our fellow men, and in doing this take into account to varying degrees of detail, size, conformation, carriage, gait, hair, colouring, modes

of dressing, and especially facial features. This, however reflects our habits of use of our sense organs rather than any limitation of the ways in which diversity can be expressed. Not only do, for example, blind people distinguish by touch some of the features that most of us observe visually, but all of us in greater or lesser degree recognise our fellows by sound —by the intonation and pitch of voice, accent and choice of words, and even by characteristic footfalls. Differences of smell must be great before we can use them diagnostically, but dogs at least appear to be able to distinguish among human beings in this way, apart perhaps from identical twins. To the police, of course, finger prints are of special significance, for no two people are exactly alike in the patterns they show— even identical twins. Again a very large number of different blood types are recognised for their importance in medicine though—fortunately for us—we do not differ uniquely from one another in this respect. We do, however, differ uniquely in the cellular materials (antigens as they are called) which determine the reaction of our bodies to skin grafts. The result is that, apart from identical twins, skin cannot be exchanged successfully between individuals by present techniques. The treatment of, for example, extensive damage by burns is thus sharply limited by the inability to use skin grafts from any but the damaged individual himself in the initiation of the growth of a permanent new covering, though there are already indications that new techniques will be developed to overcome this limitation. These characteristics are of special significance in medicine; but in general the further we take our physiological and biochemical investigations the more differences we uncover: indeed every new technique that science devises is likely to uncover new differences among us. Not only are no two people alike, but differences which may be of any size from the gross to the trivial are displayed in every characteristic, physical, physiological and psychological that we possess.

What causes this diversity? What is its significance? For many purposes of daily life it is sufficient to recognise the differences which so obviously exist without a deeper understanding of their causation; but for other purposes—the maintenance of health, the treatment of disease, the control of crime, the planning of

education, the promotion of well-being in our communities, and the efficient utilisation of our human resources—we need to know more. Unless we understand how our differences come about we cannot appraise them, reduce them, build on them, or know ourselves and our societies in any true way.

To seek such an understanding is no new ambition. Human diversity has been the subject of interest and speculation since the beginning of man. It has been accepted as inevitable and bewailed as unjust. It has been made the basis of reverence and of persecution. It has been attributed to divine creation and to diabolical intervention. It has been traced to heredity and to the environment, to ancestry and to upbringing, often with a gross distortion of the evidence and a perverse interpretation of the conclusions. As often as a cause has been suggested its refutation has been attempted, and generally successfully in relation to at least some of the differences it was advanced to explain. For perhaps the commonest mistake has been to seek a single paramount cause of diversity, instead of admitting a multiplicity of causes whose consequences might be various and whose interplay complex.

Heredity and Natural Selection

Though the interest is ancient, the scientific study of diversity, whether in man or other living creatures, is recent. Indeed the basic techniques and notions necessary for such a study began to come available barely a hundred years ago, with Darwin, Mendel and Galton. Their development into a tool powerful enough to give us an insight into the nature of wild populations and the forces that mould them has taken place only in the last few decades, and even now we are only at the beginning of their effective application to man.

Mendel's contribution was to found the science that we now know as genetics. He gave us the basic technique of investigation and the first principles of the science. Above all he showed that the hereditary materials must be particulate or atomistic. Previously it had been thought that the hereditary contributions of the parents blended like ink and water in their joint offspring, never to be unscrambled again, so that the parental differences were irretrievably lost on crossing. Mendel

showed that this was not the case, and that the introduction of dissimilar factors (as he called them, or genes as we now say) from the two parents into their joint offspring did not result in any change of the factors themselves. These factors could and did sort out, or segregate to use the geneticists' term, in the production of later generations, in much the same way as balls of different colours can be put together in a bag and subsequently taken out without their colours having been altered by the juxtaposition. This shows us at once how heredity can determine differences between relatives as well as similarities and indeed the general principle is of fundamental importance for understanding populations.

Mendel's approach was out of the scientific fashion of his time and so his work was completely neglected for thirty-five years. With the twentieth century, however, it came into its own as the foundation of the complex structure of modern genetics. In later chapters we shall enquire further into the findings of genetics and their implications for the properties of living populations.

Genetics and its techniques enable us to explore the causes of diversity. Darwin gave us a criterion by which to judge its significance. He pointed out that, in principle, diverse individuals, whether plants, animals or men, must because of their diversity differ in their capabilities of meeting the demands made on them by the environment in which they have come into being and lived their lives, and that these differences in adjustment, or adaptation, to their environment must result in differences in their prospects of leaving descendants—in their fitness as he put it. The fitter would in general leave more descendants, so that the characteristics to which they owed their fitness would tend to spread and eventually become fixed in the population of organisms, at least in so far as these characteristics were hereditary. Thus some characteristics would be favoured at the expense of others and this process, which he called natural selection, would bring about continuous even if slow changes in the characteristics and features of living creatures, so long as there continued to be a supply of differences upon which natural selection could act. This change we recognise as evolution.

In contrast to those of his contemporary, Mendel, Darwin's principles made an immediate appeal; and not only to biologists, for the first edition of his book *The Origin of Species*, in which these principles were developed, sold out as soon as it appeared on the book-stalls towards the end of 1859. At last the significance of diversity was clear and at last causation had been set firmly in the centre of biology. Indeed it had, but never can anything have been more distorted in use or prostituted in aim than were Darwin's principles at the hands of his disciples, biological and lay alike. To read much of the late nineteenth century literature of biology is to read a catalogue of the most fantastic interpretation of living creatures and their structures in terms of alleged adaptations. And to read the perverse appeals to natural selection—with catchwords like "nature is red in tooth and claw" and "the weakest goes to the wall" and "omelettes can't be made without breaking eggs"—to justify the most meritricious arguments of politics and economics is even worse. An end there had to be to it, so just as Mendel was coming in at the beginning of this century, Darwin was going out. At first even the findings of the growing body of geneticists were taken as incompatible with the idea of natural selection and only gradually did it become realised that genetics was in fact putting in place the missing pieces of Darwin's puzzle, by giving that understanding of processes of heredity which the appreciation of natural selection and its consequences clearly required. Today the notion of natural selection is as much a part of genetics as Mendel's principles themselves, as we shall see when we come to consider the behaviour of hereditary differences in human populations.

There can be no doubt that natural selection in fact occurs. The selective predation of moths by birds has been filmed. Differential survival under conditions of competition has been observed in fruit flies. Differences in ability to withstand inclement conditions has been recorded in sparrows. The list of cases where natural selection has been seen at work is now very long and it includes clear examples in man, to which again we shall refer later. In many cases, however, interpretation in terms of adaptation is necessarily still a matter of hindsight and even surmise. Sometimes the inference is clear: there could

be little doubt for example that the layer of blubber beneath a whale's skin is an adaptation to life in cold water even though we have never actually observed that whales with a thinner layer of blubber tend to leave fewer descendants than their better protected fellows. In the same way, because he has a smaller area of body surface relative to his body volume, the short-limbed stocky-bodied esquimo would seem better fitted to withstand the loss of body heat than the longer-limbed more loosely built negro. The inference is thus fairly obvious that the esquimo is adapted to life in a cold climate even though we have no direct evidence of the natural selection to which development of the adaptation is referred. At the other extreme some characters appear to be so trivial that to regard them as adaptations resulting from the past action of natural selection can be little more than an act of faith. It should be observed, however, that to regard them as so trivial as to be devoid of adaptive significance in the absence of observational or experimental evidence is equally an act of faith. The danger in such a case is at least as great in denying all adaptive significance as in insisting on it. Has the detail of distribution of hair on a man or a fruit fly an adaptive significance? Has it in fact had an influence, albeit only a small one, on the organism's fitness to meet the demands of its environment in the past? Some of us would suspect that it has, though we cannot be sure. But equally no one can be sure that it has not. It is indeed hazardous to deny that a character has an adaptive significance and to insist that it is neutral in respect of selection, just because we cannot easily imagine it to be of any importance.

The variability of individuals can pose just the same dilemma. Sometimes we can see that the capacity for different development in different environments must be a positive advantage to the individual, as where a plant develops cut leaves under water but entire leave above it. In such a case the variability can properly be regarded as an adaptive plasticity of development, enabling its possessor to exploit a range of environments in any of which he may find himself. At the other extreme, however, variability may be nothing more than an expression of an ill-regulated system of development, so poorly buffered against external hazard as to be pushed around by even the

minor vicissitudes of life, with consequences that in no way fit the individual better for existence in that environment. Again there is the dilemma of interpretation: should we seek an adaptive significance or deny it? Sometimes there is the evidence of comparison to guide us one way or the other; but in the absence of such a guide, to deny can be as hazardous as to affirm. Darwin has indeed given us a criterion by which to judge the significance of diversity and plasticity, yet we should recognise that it is a criterion not always easy to apply: it should be no more used wantonly than denied blindly.

The Measurement of Variation

Sooner or later any science must become quantitative if it is not to languish. The quantitative treatment of populations is achieved partly by the methods of demography, which enable the age structure and fertility in relation to age to be described and analysed. Demographic methods are, however, but little used in other relations. When seeking to assign diversity to its causes or to consider its consequences the quantitative methods used stem essentially from the work of Darwin's cousin, Francis Galton. Galton set out to elucidate the mechanism of heredity, ignorance of which he could see to be the greatest weakness of his cousin's theory of evolution. To this end he studied the variation in such characters as stature in human parents and offspring. He was able to show that there was an hereditary element in the determination of stature, but the mechanism of hereditary transmission eluded him: indeed the characters and approach he used virtually foredoomed his attempt to failure. He was, however, led to devise ways not only of representing and measuring the variation he found among the people he measured, but also of analysing the resemblances, or covariation, it revealed between relatives, and perhaps most important of all he put us on the way to thinking constructively about variation. So began biometry, the science of quantitative biology.

Now, all biological phenomena are variable. An observation or experiment is never repeatable in exact detail, for it is subject to the influence of a host of agencies, extrinsic and

intrinsic to the organism, which affect its outcome in greater or lesser degree. These agencies cannot all be controlled even in an experiment and indeed many or even, for all we know, most of them may not be recognisable. So we must measure the overall variation due to all these other causes as well as the differences relatable to the agencies about whose effects we are enquiring. Then by comparing the two we can form an idea of whether the latter are sufficiently large and important, or significant as the statisticians would say, for us to feel confident that they are not just the misleading expression of some uncontrolled or even unrecognised source of extraneous disturbance. Our conclusions always emerge as statements of probability. Even the largest effect apparently relateable to the agency in which we are interested *might* be due to the extraneous factors; but if the chance of it having come about in this way is small, we can feel some confidence that the agency of interest is having its effect, and the smaller the chance of the one the greater our confidence in the other. Thus, to take a very simple illustration, if when comparing the average stature of a group of Englishmen, taken at random, with that of a group of Japanese we find a difference, we must ask whether it is merely a reflection of the differences that we should in any case find among groups of Englishmen or of Japanese or whether it is too large to be assignable reasonably to this cause. We can work out the probability of it arising solely from the variation within the races and so arrive at a basis for deciding whether we must postulate an overall or average difference as existing between them.

This approach, developed and elaborated in its mathematical application especially during the last forty years or so, is now basic to the interpretation of biological data and has indeed spread well beyond the bounds of biology into all fields of science dealing with variable phenomena. It is now, for example, the foundation of operational research in industry. Its power is attested by the success it has achieved in so many fields of enquiry not only in the interpretation of results but also in the insight it gives into the designing of experiments deliberately to yield results clearly interpretable and meaningful in relation to the questions being asked. It has also led us to a

deeper insight into the nature of the inductive reasoning we use when arguing from particular observations to general conclusions. There must always be the risk that our particular results do not afford a sound or unbiased basis for a general statement. This is reflected in the statement of probability which the analysis yields. The conclusions are not certain, and such conclusions clearly can never be, but as our body of observational experience grows the uncertainty becomes less.

This inductive, or uncertain argument (non-certain argument would perhaps be a better term) stands in contrast to the deductive, or certain, argument that we are all taught in the form of Euclidean geometry as a matter of course during our school-days. There we argue from the general to the particular, and given the initial premise the particular consequence must follow. It is easy to confuse lack of certainty with lack of rigour and in consequence to deny the validity of conclusions stateable only in terms of probability. Yet uncertain statements can be quite rigorous. To take once again the simple illustration of stature in man, we cannot say with certainty what the stature will be of the next man we meet, but armed with knowledge of the variation in stature of our population we can say quite precisely what the chances are that he will be of a stature between 67 inches and 69 inches or 72 inches and 72½ inches or 150 cm and 157 cm. or whatever other range we choose to take. We can in fact make clear, meaningful and valuable statements about his size—as anyone who is stocking a shop with ready-made garments is obviously recognising.

So, joining the techniques of biometry to the findings of genetics and the principle of natural selection, we can proceed to the study of diversity, its causes and its significance. In doing so we shall be concerned with populations as much as with individuals, for when dealing with variation the individual, whether it be individual organism or individual observation, is no longer an adequate unit. The causes express themselves by effects on individuals and the consequences will differ with the individual but we can only come to understand how the causes work and what form the consequences may take if we look at them as they act and appear in populations.

2

Causes of Diversity: The Environment

Every living creature receives from its parents an endowment of hereditary materials—its genes. Equally it must pass through all the stages of its development in some environment or series of environments. So every living creature is the joint product of the genes it receives from its parents and the circumstances in which it grows up and lives its life. In genetical language its phenotype (the type that is seen) is the resultant of its genotype (the type that creates) and its environment. So no feature or character of an organism can be said to be brought about entirely by the genes or entirely by the environment: both are always at work. It is, however, possible to ask whether a difference between two individuals is traceable to a genetical difference between them, or to a difference in their environment, or of course to both causes acting simultaneously.

Geneticists are always asking this question and they have accumulated a vast amount of information from the answers they have obtained about all sorts of characters in all sorts of organisms, simple and complex, plant, animal and human. In brief, they have found, first that all characters that have been studied seriously in all organisms show genetically determined differences, and second that almost all characters show environmentally determined differences. Sometimes the genetical differences show up only in certain environments, or the effects of differences in environment are displayed only by individuals of particular genetical constitutions. Then the differences we see are said to result from the interaction of genotype and environment. But in the vast majority of cases both genes and environments are capable of causing differences in the character. The exceptions are characters like blood-type: so far as present knowledge shows, these are almost completely

insensitive to effects of the environment, so that their differences are virtually always referable to the genes.

So, in general we must expect the diversity we see in any living species to spring partly from genetical and partly from environmental causes. Virtually every character is subject to both types of effect and, what is more, our experience shows us that genetic and environmental agencies may mimic one another in that they may produce variations indistinguishable from one another by inspection. The individual may develop poorly because of inadequate nutrition or because of a poor set of genes, and only appropriate observations of relatives on different planes of nutrition can finally distinguish these causes. Such observations can readily be obtained from experiments in other species, but in man the possibilities are obviously more limited. This introduces a difficulty to which we shall have occasion to return later.

In most species it suffices to distinguish between the genetical and environmental as causes of diversity. In man, however, (and in other species of higher animals though to a much lesser extent) it is necessary to take into account a third cause if understanding is to be complete. While it is true that in a formal sense each of us may be regarded as reflecting the influence of the genes he bears and of the environment in which he has developed, that environment has certain peculiar properties depending on his family and the community or society to which he belongs. These will determine to a great extent not only his physical environment, but also the education he receives, the ideas he imbibes, the conventions and customs to which he will conform (or against which he will rebel), and the activities he will pursue. His environment is thus itself partly hereditary and what he obtains from it he can in part pass on again. He does so by a process of transmission which itself is not that of heredity, though it may operate most powerfully among relatives, who by reason of the special place of the family in our society, are most open to one another's influence. That which an individual receives in this way from others may be altered as a result of his activities, his experience and the ideas he has as a result of that experience, before he in his turn transmits it. Thus this process of social transmission, as we may call it

to distinguish it from genetic transmission, provides an environment both physical and social which in itself is capable of progressive change and to the progression of which each individual, himself the beneficiary of it, may make his own contribution. It provides in fact a means of social evolution which can proceed independently of the biological evolution arising from progressive adaptation favoured by natural selection and transmitted by the genes.

The capacity for social evolution is, however, rooted in the biological. It requires that an individual is prepared to take trouble for the welfare of others. Within the narrower sense of physical needs and within the restricted community of the immediate family, parental care shows us such behaviour as a feature common to many species. Indeed the development of means of protecting and nurturing the embryonic offspring is a feature of plant evolution as it is of animals. Mere parental care, however, even where it goes beyond the provision of nutriment and shelter to embrace the simple education of the young, is but an adjunct of heredity: it benefits only those who have received the donor's genes and it may properly be regarded as no more than an extension of the process of reproduction which is thereby rendered more effective because the offspring are given a better start in life. Social transmission as we know it in man, on the other hand, is not limited to the parent-offspring relation: it does not stay within the family, even though it may be strongest there: it is not always from the older to the younger, even though this may be the easiest and commonest direction for it to take. Nor is it limited to the meeting of physical needs: indeed in man, the most important provision is of education, using this term in its very broadest sense to cover the transmission of information, ideas, forms of behaviour and beliefs of all kinds. It is therefore at once a property of the community and a thing of the mind.

Now clearly, social evolution and its chief agent, education, make certain demands on the individual, notably the mental capacity for it as well as the preparedness to learn and teach. To these may be added the means to communicate at the necessary level of complexity. These means are themselves a product of social evolution, and as such again demand a certain

minimal level of mental capacity; but they also obviously make physical demands on various organs of the body including the sense organs. Finally we may include the necessary physical skill as well as mental capacity to make and use devices or tools, since although this could in principle be a purely individual activity independent of social communication at least at a low level, it is in fact so bound up with communication and communal activity and so essential a part of social evolution as we know it that the propriety of its inclusion can hardly be doubted. All these capacities, mental and physical alike, are biological properties of the individual. Individuals vary in respect of the extent to which they possess them, and the variation arises partly from genetic and partly from non-genetic agencies. In classifying the causes of human diversity into the environmental, the genetical and the social, therefore, we must be prepared to find a complexity of interplay among them in the production of their effects and the significance of their changes. This interplay will emerge as we proceed to consider the three classes in turn.

Environment: The Balance of Population

With but few exceptions all human characters and characteristics are affected by the environment. They are therefore all liable to alteration in greater or lesser degree if the environment is changed appropriately, and if the relevant agencies can be distinguished in the environment quite specific change can be brought about in the individual by their manipulation.

Each of us requires from his environment foodstuffs of an appropriate kind, shelter from the elements and protection from other external harm. In childhood and in times of illness or other upset these demands become more rigorous and take on a special nature. The effects of change in these environmental agencies are too striking and too well known to require detailed exposition. With the discovery of vitamins, the elucidation of dietetic needs and improvement in the availability of food supplies, the nutritional status of the populations has risen markedly especially in the western countries. Health is better, deficiency diseases rare and rate of growth greater.

The change is especially noticeable in children, whose average stature, age for age, has risen steadily during this century, even though final stature may not have increased. Children mature earlier too. If contrast is needed to point the change it is provided by the many peoples of Asia and elsewhere who are still living at a bare level of subsistence and whose physique and rate of growth display their low nutritional status. It is worth observing, too, that as nutrition has improved in the western countries the diversity from differences in nutrition among their populations has diminished in respect both of physique and of general health. Improvement has been effected by a levelling upwards.

Improvement in nutrition has been accompanied by similar changes in general standards of clothing and housing. Perhaps the greatest change in respect of the latter has been the development of adequate levels of sanitation. This, together with other measures of preventive medicine has virtually eliminated many infectious diseases which were recurrent in the nineteenth century or even only a few decades ago. The control of such diseases is being extended steadily by a variety of means of which the most striking of recent time has been the use of new insecticides to kill out the insects carrying and spreading parasites like that responsible for malaria. For all its development, curative medicine has been a much less potent factor than preventive medicine in raising the general standards of health.

The very success of improvement in nutrition, housing and the control of disease brings its own problems. The immediate effect of these measures is a reduction in the death rate. Then, unless the birth rate falls correspondingly, there must inevitably be a rise in total population. Now if the effect were merely to prolong the average life of each individual born without affecting the numbers reproducing, the increase in the size of the population would be self-determining, for everyone born must sooner or later die and a doubling of the average life span would simply result ultimately in doubling the size of the population. Another factor, however, enters in. If a population is to be stable in size over the generations, each pair of parents in one generation must on the average leave two

offspring to breed as parents in the next. The average number of all offspring would of course be greater than two, for failure to survive or to breed would eliminate some of them from the count. In the past in countries like our own many children have been born to each parent, but inadequate nutrition, disease and other causes have reduced these to something like

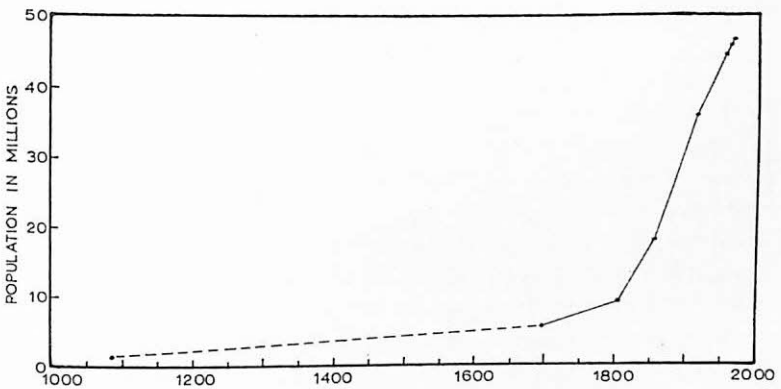

FIG. 1. Growth of the population of England and Wales.

the mere replacement rate required by equilibrium of population size. Thus the best estimates we can make suggest that despite a high birth rate, the population of England and Wales rose on the average only slowly for a period of several centuries (see Fig. 1).

With the late eighteenth century a change set in and the population began to increase sharply. The precise reason is a matter of dispute. Some insist that as a result of improved economic conditions the average number of children born to each parent increased. Others point to the more likely possibility that out of the same number of children born a greater proportion survived to reproduce in their turn. However this may be, the number of children surviving to reproduce exceeded that required for simple replacement and stayed in excess of this requirement throughout the nineteenth century. Under these circumstances not only did the population rise, but it inevitably continued to rise generation after generation

and at a prospectively increasing rate. With the twentieth century, however, the birth rate fell, so that even with the greater prospect of survival of each child to reproduction, the numbers so surviving fell first to, and between the wars even just below, the replacement level. Despite this fall of the birth rate below the replacement level the population itself continued to rise because, of course, it takes a whole life span for an equilibrium of actual numbers to be struck within a population and the mere prolongation of life necessarily prolongs this period. Nevertheless with the birth rate at its level of twenty or thirty years ago, the population must sooner or later not only have contained a greater proportion of old people, but also have actually begun to decline. In fact the birth rate has now risen again, as it has done virtually simultaneously in all the western countries, so that numerical decline has been at least postponed and perhaps finally avoided.

The early stages in these changes in our English population must in some measure remain matters of conjecture since detailed statistics of births and deaths were not compiled. The later stages are made certain by the official records which began in the last century. The picture that emerges clearly shows the inter-relation of birth rate, survival rate and population size. Unless birth rate and chance of survival to reproduce are such that taken together they just achieve the average replacement of each pair of parents in one generation by a pair in the next, the population must change in size, upwards if the replacement rate is exceeded and downwards if it is not achieved. We cannot be completely sure, but the rise in population appears most likely to have resulted from a rise in the chance of survival of a child to reproduction (or a fall in the early death rate if we choose so to express it). The levelling out a century or so later was due to a fall in the number of children born, sufficiently great to offset the rise in chance of survival. The threat of reduction in population size arose when the fall in number of children born was so great as more than to offset the rise in chance of survival.

We know how a rise in chance of survival is brought about: by the amelioration of the environment, through the reduction or elimination of famine, disease and other hazards to the young.

We do not know just why the birth rate in western countries subsequently fell, whether it was for economic reasons, the development of notions of social prestige, the raising of the status of women in the community, education, the availability of means of birth control or any combination of these. Nor do we know why the birth rate has recently risen somewhat again. In other words we know how to manipulate one side of the balance, but not the other. In Asia and elsewhere we have been manipulating this side of the balance by improving nutrition, lessening famine, and improving medical care. The chance of survival of children to reproduce has gone up. The birth rate has not gone down. So the population is rising and threatens to go on doing so almost explosively if the birth rate does not come down—so long of course as the increasing population can be fed and cared for well enough to prevent a fall in survival rate restoring the balance. Efforts are being made to find ways of reducing the birth rate, but without any noticeable success so far. Indeed in Japan abortion has been legalised either to prevent birth or to reduce the chance of survival, whichever view one takes according to whether one regards birth or conception as the more significant biological event. Yet the population still grows. And the more it grows the greater the struggle to provide food and care to prevent the chance of survival falling and thereby to keep numbers growing still further. Our sense of the humanitarian requires us to do this; but we must be clear about the consequences. So long as the balance remains upset, so long as we have no way of inducing a reduction in the birth rate of these populations, so long will they continue increasing in numbers until ultimately the maintenance of food and care will get beyond us. That is our dilemma. It is the greatest problem facing mankind at present, and our greatest need is a knowledge of how to manipulate birth rates as we manipulate food supplies and control disease. And the problem is not made easier, nor the situation alleviated, by deliberate encouragement, whether from church or state, to maintain and even increase birth rates already sufficiently high to exceed the requirements of replacement under the circumstances which now prevail.

Environment and Disease

Our improvement of nutrition, housing and the control of disease has upset the biological balance upon which depends population size. It must also have upset other though less obvious biological equilibria. We have, for example, every reason to believe that an individual's ability to resist infection depends in part on his genes. This is a genetical commonplace in other species and indeed one of our standard ways of arming our domestic plants and animals against disease is deliberately to breed for such resistance. We must expect man to show the same genetical diversity in disease resistance and we have in fact direct evidence that relatives tend to resemble one another in their resistance or susceptibility to diseases like tuberculosis, the closer the relationship the greater being the resemblance (Fig. 2). We also know that, no doubt at least partly for genetical reasons, the introduction of a disease has had disastrous effects on populations previously not exposed to it, as when the diseases of civilisation reached Tierra del Fuego in the last century[4]. In a population continuously exposed to the ravages of an infectious disease, as for example ours was exposed to bubonic plague or smallpox, there will be a steady pressure of selection in favour of those carrying genes conferring a measure of resistance, and therefore a selection in favour of the genes themselves. As soon, however, as the disease is controlled and even virtually eliminated, this pressure of selection will wane and we should expect the genetical situation gradually to change. The genes for resistance must be expected to become rarer as the chief factor encouraging their maintenance and spread is removed. We do not know how rapid a process this would be, for genes are not the only factors concerned in disease resistance. We do not even know for certain whether in fact our expectation has been realised at all in man, for with the elimination of the disease our direct means of assessing susceptibility to it has obviously gone also. Few geneticists would, however, doubt that it must have occurred and later we shall see direct evidence of just such an effect springing from medical treatment, though of an organic rather than infective upset.

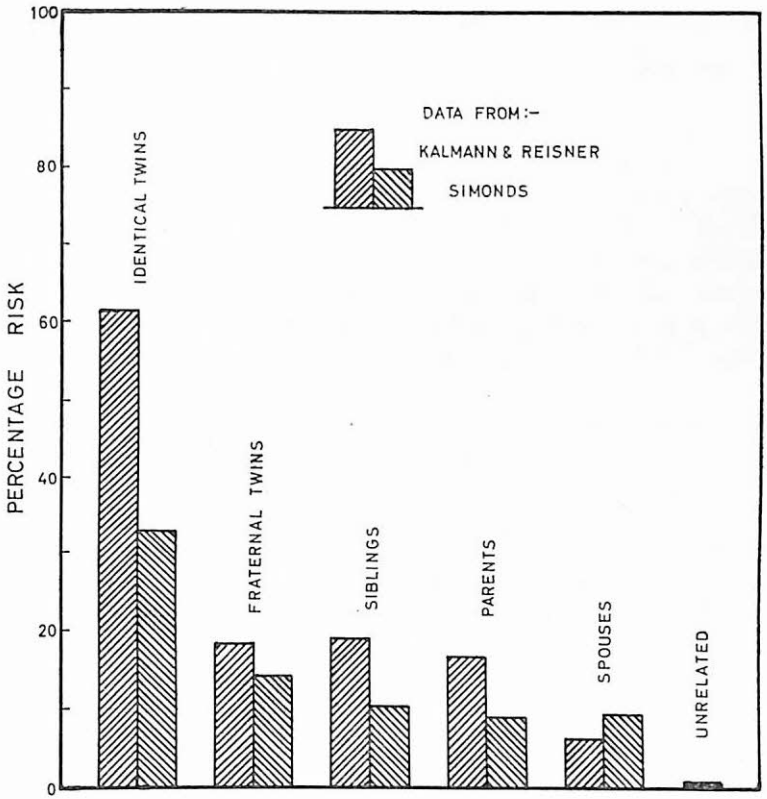

FIG. 2. The risk of developing tuberculosis among the relatives of individuals who have contracted the disease. It is very high among identical twins who, of course, have exactly the same genetical constitution as the affected individual. It is less high among sibs (i.e. brothers and sisters) and offspring, though still much higher than among the unrelated individuals of the general population. While displaying in this way the genetical determination of susceptibility to the disease, the figures also show the part played by infection. Parents and offspring are genetically as much alike as sibs yet the incidence is less, no doubt because the risk of transmitting actual infection is less than between sibs. The higher incidence among spouses than among unrelated members of the general population would also seem to reflect a higher risk of infective transmission. While it is possible to see both influences at work it is difficult to assess their relative effects, because the risk of transmitting the infection will generally tend to rise with the genetical relationship. The differences between Kallman and Reisner's [16] figures and Simonds' [33] reflect a difference in the mode of ascertainment of the twins.

Such a genetic change resulting from an amelioration of the environment is of little more than academic interest so long as the environment is maintained at its new level: lack of genes conferring resistance to a disease is no handicap so long as there is no exposure to the infection. Only if the environment deteriorated would the genetical change become significant. It is however important to observe that whereas changes of the environment can often be brought about rapidly, the benefits they confer last only as long as the changed environment is maintained. The improved physique arising from adequate nutrition or the freedom from cholera springing from good sanitation, lasts only as long as the food supply or the drainage system. Genetical changes in the population on the other hand, by whatever means they are brought about, are generally slower to develop but also persistent in their effects, for unlike the food supply or the drains, the genes upon which they depend are passed on from generation to generation come what may. It is to the genes, the diversity they cause, the equilibria they strike and the changes they undergo, that we must now turn.

3

Genes and Diversity

Man is a difficult subject for genetical study: his families are small, his time between the birth of one generation and the next is long, and his matings are genetically uncontrolled, so that information essential for the establishment of a genetical point may be exceedingly troublesome to obtain. It is frequently difficult even to establish the precise mode of inheritance of a variant character. This is especially the case where it is suspected that similar modification of the phenotype may be produced by changes in more than one gene. The relationship of the changed gene is easy to test in an experimental plant or animal where individuals from the different lines may be crossed at will; but the most we can do in man is to search hopefully for the critical mating and if, as is not infrequently the case, we fail to find it we must fall back on such indirect and seldom fully conclusive evidence as may come available.

This is but an example of the kind of difficulty which can beset us in the genetical study of man. Indeed human genetics could hardly have developed at all if the experimental genetics of other and more tractable species had not been available to provide the foundation on which to build. We know, however, that the fundamental laws of inheritance are virtually universal in their application. They are the same in fungus as in fruit fly, in mouse as in maize plant, and it would thus be remarkable indeed if they did not hold good in man. The experimental study of other species, therefore, tells us what we should expect in man, and knowing what we are looking for we can establish the applicability of principles that would have been impossible to discern without such a guide. We know now that man has basically the same chromosome apparatus as other species, that his sex is determined by the combinations of the so-called

sex-chromosomes in essentially the same way, that his genes are borne on his chromosomes and that he displays all the classical genetical phenomena of segregation, linkage, sex-linkage and so on. We know too that man's genes change or mutate, and that his chromosomes sometimes behave aberrantly, for reasons and with consequences that had earlier been established in other species. And we know that these changes in chromosome and gene affect the fitness of the individual displaying them, so that natural selection is at work in man as in other living creatures. Furthermore, every time we establish that man provides no exception to a genetical rule we fortify our confidence in the applicability of new genetical findings to ourselves. Our evidence is, in fact, that for these genetical purposes human populations may be regarded just like wild populations of any other naturally out-breeding species and that we must expect the same basic rules and principles to apply, though the detailed consequences of their application may reflect also the biological peculiarities of mankind and the organisation of his societies.

Whatever the difficulties of its genetical analysis, diversity is better known in man than in any other species, as indeed might well be expected. Experience of it confirms the great principle we have already had occasion to observe, that all characters and traits, physical and physiological, mental and morbid, show heritable variation and that the great majority show environmentally determined differences as well. Any character showing environmental variation can in principle be changed deliberately by external intervention and, as we shall see, this in turn means that genetical upsets can be alleviated or even remedied by an appropriate treatment if this can be discovered. Such intervention in its turn affects the genetical situation with consequences that we must examine in due course. For the moment it will suffice to observe that all human populations display variation in all the characters that have so far been adequately examined.

Broadly speaking there are two types of variation; the discontinuous in which the diverse types stand in clear contrast to one another, with intermediates rare or absent; and the continuous in which the diversity is essentially quantitative

or metrical, with every gradation in expression of the character between wide extremes, the intermediate types being the most common. The genetical element in discontinuous variation usually springs from a very few gene differences of major effect. Thus achondroplasiac dwarfism, haemophilia and phenylketonuria with its associated mental deficiency, to take but three examples of abnormality, differ from the normal in only a single gene. Similarly the common differences in blood group depend on a very few genes each with its own specific effect, and the differences between the sexes are largely brought about by a single unit of inheritance, though in this case the unit is a whole chromosome. Continuous variation, on the other hand, is usually determined by a whole system of genes whose individually small and unspecific effects sometimes balance one another out and sometimes supplement one another to produce large differences. The manifestation of the character is thus dependent more on the number of genes pulling in each direction, towards higher or lower expression, than on just which of the genes the individual happens to possess. The effects may further be modified by environment agencies, so that it can be a matter of no little complexity to measure the extent to which the continuous variation of a character is genetical as opposed to environmental in origin.

Both discontinuous and continuous variation may be displayed by the same character. The variation in stature that we see about us every day in our fellow men is continuous: if we measure a sufficiently large sample of people we find every gradation between wide extremes with the statures near the average as the most common. The only gross difference is that associated with sex, women being on the average several inches shorter than men, though of course the ranges and distributions of the sexes overlap, some women being well above the male average and some men shorter than the female. If, however, we go to the circus we see examples of discontinuous variation in stature, for the dwarfs there generally owe their peculiarities to the large effects of specific single genes, including that for achondroplasia, already mentioned. Similarly the differences in intelligence that we know from daily life follow a continuous distribution similar to that for stature,

the very bright and the mentally backward being merely the opposite ends or tails of this continuous range (Fig. 3). But the very extreme mental defectives generally owe their condition, where it is genetically determined, to the gross effects of single genes like that for phenylketonuria. There is,

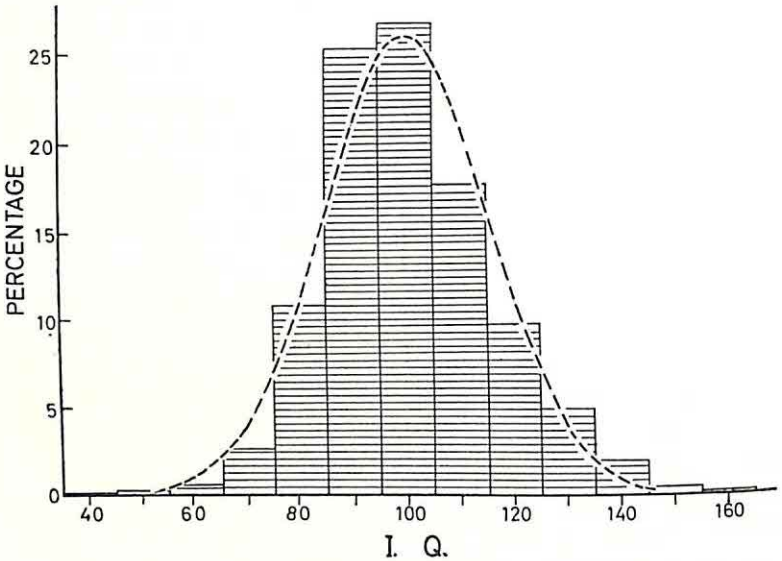

FIG. 3. The distribution of I.Q. among the 14,963 children born in Scotland on 1st February, 1st May, 1st August and 1st November 1926. The shaded histogram shows the percentages of the group with I.Q.'s lying in the ranges 35-45, 45-55, 55-65 · · · 155-165. This grouping into ranges of 10 points of I.Q. is artificial and is done solely for ease of representation: it does not imply any discontinuity in the value of I.Q. that children can show. The broken curve shows the ideal distribution calculated from the observations and representing the statistical population of which the children actually observed are regarded as forming a sample. (Date from MacMeekan [18]).

however, no evidence of corresponding single genes endowing their possessors with intelligence greatly above the normal range. Evidently single gene changes of gross effect can degrade a character but not enhance it: they are vastly more likely to damage the machinery of normal development than to improve it. Improvement in this as in other characters must in fact

generally come from the accumulation of small favourable effects just as Darwin saw a century ago.

It is convenient to draw a distinction between discontinuous variation, mediated by one or a few genes of large and specific effect, and continuous variation, mediated by a system of many genes (a polygenic system) of small, similar and supplementary effect. The distinction is not, however, final or complete. Discontinuity in expression may arise from the very nature of the character itself and conceal an underlying continuity of variation in the potential effect on the character, as must be the case for example in the determination of the number of teeth we possess: this number can vary, but obviously only by at least one at a time no matter what the nature of its genetic determination. At the same time gene changes themselves are not simply classifiable into those of large and small effect: their consequences may in fact be of any magnitude from so large as to bring about death at a very early stage of development to so small as to escape detection by any but the most refined and extensive observation. Furthermore, the same genic structure may change in different ways to produce large specific effects and small non-specific effects on different occasions, and the same change may even bring about simultaneously a large effect on one character and a small effect on another. The two types of variation are nevertheless broadly distinguishable and they are of different significance for the occurrence and maintenance of diversity in human as in other populations. We shall therefore consider them separately in seeking answers to the questions of how genetical diversity comes about and of how it is effected by the actions and activities of selection.

Chromosomes and Genes

Normally each of us possesses 46 chromosomes. In a woman these fall into 23 pairs the members of a pair being similar, or homologous as it is termed, in respect of the genes they carry and the order in which these genes are arranged along the chromosome. The 46 chromosomes may thus be regarded as comprising two homologous sets, each of 23 different

members. One set of 23 is derived from each parent and a set of 23 is passed on to each offspring. The set passed on is not, however, exactly like the set received from either mother or father, as the production of germ cells (eggs in a woman and sperm in a man) involves the random distribution of the members of each pair of chromosomes. Thus the germ cell which an individual produces and which bears the hereditary contribution that individual makes to his offspring, will carry some chromosomes originally derived from the individual's mother and some derived from his father. Furthermore, the members of a pair of chromosomes may during the production of germ cells exchange material by a process known as crossing-over so that even a single chromosome as passed on to the offspring may carry genes of both maternal and paternal origin. There is thus a constant reshuffling, or recombination, of genes by the sexual process (Fig. 5).

The situation in a man is just the same as in a woman in respect of 44 of his 46 chromosomes. These fall into 22 pairs of homologues. The members of the 23rd pair are not, however, alike. One is the same as the members of the corresponding pair in a woman and is known as the *X* chromosome. The other is much smaller, does not carry the same content of genes, and is chiefly responsible for its possessor being male. This is the *Y* chromosome. The *X* and *Y* in a male are alternatives in the sense that one or other is passed on to each offspring. Now a woman must pass on an *X* to each of her offspring. Two kinds of progeny will therefore be produced, all getting an *X* from the mother but one receiving an *X* and the other a *Y* from the father. Thus the two kinds will be *XX* and *XY* respectively so giving females and males again in approximately equal numbers.

Certain genes are carried only by the *X* chromosome, and have no counterpart in the *Y*. A girl derives one representative of each such gene from each of her parents; but a boy obtains his sole example from his mother, so that his constitution in respect of *X*-borne genes depends only on his mother. This is the basis of the peculiar sex-linked type of inheritance shown for example by certain types of colour-blindness and by haemophilia, which indeed has been transmitted almost entirely by females while being displayed almost exclusively by males.

Genes carried by the *Y* chromosome would be handed on entirely in the male line, but apart from those concerned with maleness such genes are, to say the least, very rare in man.

Occasionally things go wrong with the mechanism of chromosome behaviour, and instead of the normal single member of each pair, an offspring receives from one parent both members of one of the pairs of chromosomes carried by that parent, or alternatively neither member of the pair (Fig. 4). The number

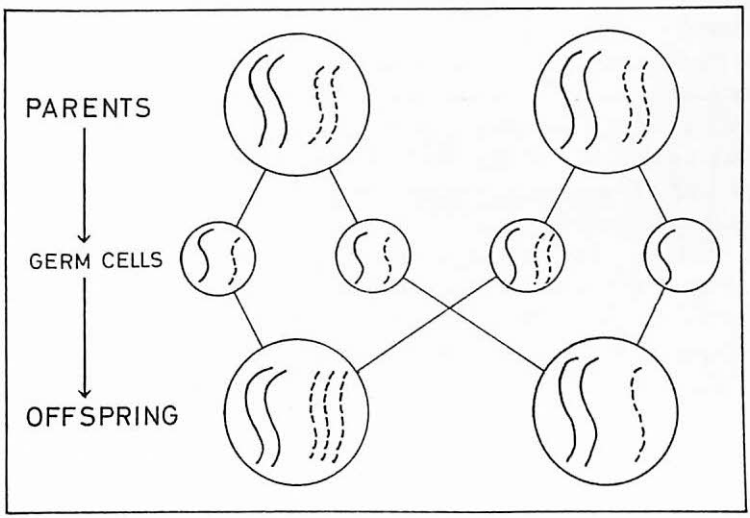

FIG. 4. Normal and aberrant chromosome behaviour. Characteristically each germ cell (egg or sperm) receives one member of each pair of chromosomes, with the result that when a new individual is formed by the fusion of an egg and a sperm it has a pair of each kind of chromosome, one member of the pair stemming from each parent. This normal behaviour is illustrated by the chromosomes portrayed as solid lines. Very exceptionally, both members of a pair of chromosomes pass into a single germ cell, another germ cell correspondingly receiving no member of the pair, as illustrated by the chromosomes portrayed as broken lines. If such germ cells function, individuals are produced having either three or only one of this type of chromosome in place of the normal pair. The former type is said to be *trisomic* and the latter *monosomic* for the particular chromosome and both are liable to be grossly abnormal in development. For example, trisomy for the chromosome known as no. 22 results in the individual developing as a mongoloid idiot.

of chromosomes, and with it the content of genes, is then abnormal and the individual may display the upset in a way characteristic for the particular chromosome involved. Some of these abnormal chromosome constitutions appear to produce such gross upsets as to prevent full development. In other cases development proceeds but the individual is abnormal. Thus a child carrying three instead of the normal pair of one particular small chromosome characteristically develops into a mongoloid idiot. Where the abnormal constitution is of the sex chromosomes, an *XXY* individual displays the Klinefelter syndrome of abnormality and an *X* individual the Turner syndrome, sexual development being upset in both cases. An individual bearing only a *Y* chromosome, and hence entirely lacking the genes of the *X* which are normally present in males as well as females, never develops. This constitution is thus said to be lethal.

Not only the number of chromosomes but also the arrangement of the genes within them can sometimes change. These alterations are, however, of importance only in special cases or in special ways and need not detain us.

Like the chromosome which carries it, each gene is represented twice in every individual—apart of course from the genes borne on the sex chromosomes in the male. One representative of each gene is derived from each parent and one representative is passed on to each offspring (Fig. 5). The two representatives of the gene are borne at exactly corresponding places, or loci, in the two members of the pair of homologous chromosomes. On this depends their behaviour as alternatives (or alleles) in the sense that because of their corresponding location one or other, but not both or neither, is passed on to each offspring. Genes at corresponding loci are alternatives in function as well as in hereditary transmission: they control the same processes as one another, and if they differ in their effects it is almost always a difference in the efficiency with which they do their work rather than in the basic nature of their action. Genes at different loci do not normally stand in this relation to one another, so that if a piece of chromosome is entirely missing from an individual, the function of the genes it carries cannot be taken up by genes in other portions of the

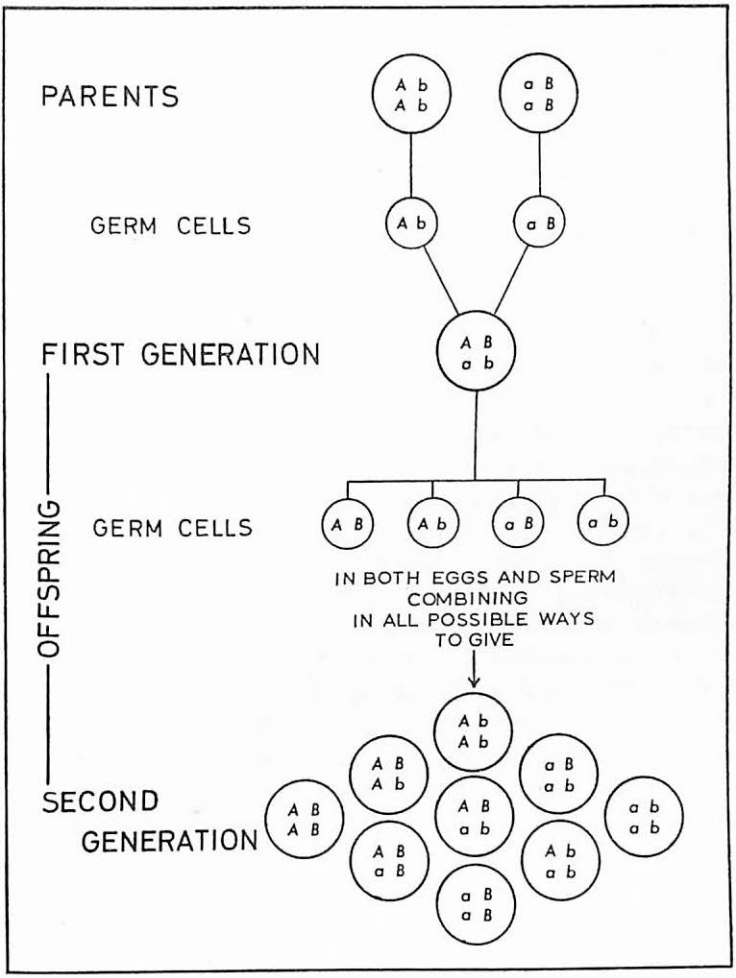

FIG. 5. Segregation and recombination of genes. Considering the alternative genes *A* and *a* (or alternatives *B* and *b*), it should be noted that the parental difference between *AA* and *aa* individuals reappears in the second generation after the cross, even though it appears to have been lost in the first generation. The reappearance is *segregation*.

Turning to the relationships between *A-a* and *B-b*, although the parental germ cells carried only the combinations *Ab* and *aB*, those of the first generation offspring carry all four possible combinations, *AB*, *Ab*, *aB* and *ab*. The second generation offspring may thus include nine different genotypes, six of which were not present in either the parents or the first generation after the cross. This is *recombination* of *A-a* and *B-b*. The same nine genotypes would have appeared in the second generation if the parents had been *AABB* and *aabb*.

chromosome material. Lacking these genes and hence the processes they determine, the deficient individual cannot survive.

Genes are normally very stable, reproducing themselves exactly during the development of the individual bearing them and being passed on by that individual to his offspring (though in reshuffled combinations) in the exact form he received them from his parents. Very occasionally, however, a gene changes or mutates. It still occupies the same locus on the chromosome so that the mutated gene is still an alternative in inheritance to its normal predecessor; but it differs from its predecessor in its action (usually, as we have seen, by being less efficient in its working) and so may affect in a characteristic way the development of the individual carrying it. It is by the production of these characteristic differences from the normal that we recognise the changed genes. The mutated gene is as stable in development and hereditary transmission as was the predecessor from which it arose by mutation.

Gene mutation goes on as we say spontaneously, that is, without artificial intervention and for reasons which we can only surmise. It can, however, also be stimulated by a variety of agents including ionising radiations, such as X-rays, gamma rays and neutrons, and also a wide range of chemical substances of which mustard gas was the first to have its mutagenic effect discovered. This stimulation reveals itself as an increase in the rate at which mutations occur and not by the nature of the mutant genes produced or the effects to which they give rise. So far as we can judge spontaneous and induced mutations affect the same genes in basically the same ways and with essentially the same range of effects on development.

Genes in Populations

What do the properties of chromosomes and genes mean for diversity in populations? Let us consider the simplest case of two genes, one (A) a mutant from the other (N), occupying the same locus in one of the chromosomes and therefore alternatives in inheritance. Let us suppose that if we take into account all the representatives of that chromosome in the population, a proportion u of them carry the normal gene and a

proportion v $(= 1-u)$ carry the mutated or abnormal gene. Let us further suppose that these proportions are alike in the chromosomes of the female and male members of the population so that a proportion u of the eggs carry N and v carry A, and similarly u of the sperm carry N and v carry A. Now, if, taking the population as a whole, the combinations in which the eggs and sperm come together in fertilisation are unrelated to the genes they carry, an N egg will be fertilised by an N sperm in u of cases and by an A sperm in v of cases, and similarly for A eggs. It is thus easy to show mathematically that the individuals of the next generation fall into the three possible types in the proportions

NN	NA	AA
u^2	$2uv$	v^2

Now the NN individuals in their turn produce only N germ cells (eggs or sperm according to sex) and the AA individuals only A germ cells. But, as N and A are alternative genes, the NA individuals produce two kinds of germ cell, half being N and half A. Thus taking the population as a whole the proportion of N gametes produced will be u^2, from the NN individuals, plus $\frac{1}{2}(2uv)$ from the NA's, giving $u^2+uv = u(u+v) = u$. Similarly the proportion of A gametes will be $v^2+\frac{1}{2}(2uv)=v$, so that the N and A genes will be in just the same proportions as at the beginning of the cycle which will thus repeat itself. So the pattern of diversity produced by these genes will go on generation after generation indefinitely. To put it another way, in respect of this pair of genes, the population is in equilibrium.

This rule of equilibrium in the proportions of the three types of individual was first worked out by Hardy in Britain and Weinberg in Germany more than fifty years ago and it is often referred to as the Hardy-Weinberg law. It depends on two assumptions:—

1. That there is no agency tending to change the proportions of the two genes.
2. That the way eggs and sperm come together in fertilisation is unrelated to the genes they carry, or to use the technical term, that they combine at random in respect of these genes.

The first assumption is not in general true, as we shall see in the next chapter. For the moment, however, we will confine our attention to the second assumption.

Assortative Mating and Inbreeding

Now the ways in which the germ cells combine in fertilisation obviously depend on the way the individuals which bear them come together in mating. Random combination of the germ cells depends on random mating of the parents, and random mating may be upset in either or both of two ways. The first is by the assortment of individuals in mating in relation to the characters their genes determine in them, so that mating may be preferentially between men and women alike in the character, or on the other hand it may be preferentially between unlikes. The second way is by the preferential mating of close relatives who, because of their relationship, will clearly tend to resemble one another more closely in the genes they carry than will two people taken at random from the population.

The most obvious example of assortment in mating being influenced by a genetically determined character is, of course, sex, for mating can only take place between unlikes. The result is a gross departure from the Hardy-Weinberg equilibrium, half the population being XX, half being XY and none at all being YY. Such an individual would not be capable of development even if fertilised eggs of this constitution were to occur; but this inability may itself merely reflect a genetical degeneracy of the Y chromosome arising as an evolutionary consequence of the preclusion by the mating system of the production of YY types as a normal occurrence.

There is no evidence of preferential mating, whether of unlikes or likes, in respect of the characters such as blood groups by which individuals are commonly distinguished into sharply distinct categories within populations. Turning to characters showing continuous variation, however, there is a marked preference for mating of likes in respect of both stature and intelligence. The correlation between mates in these characters is not complete, but the tendency is clear. Now such a tendency raises the proportions of the pure-breeding genotypes,

NN and *AA*, at the expense of the *NA* individuals in the population, and where genetic determination of the difference is by only one or two genes this effect could be marked. With continuously varying characters like stature and intelligence, however, many genes are simultaneously at work and the distortion of the Hardy-Weinberg proportions is not large for any single one of them. The chief effect of assortative mating is, in fact, a tendency towards association with one another of genes of similar effect at different loci, rather than an association of like genes at the same locus.

The genetical effects of any assortative mating, which results from similarities or differences in particular characters the individuals display, will of course be confined to the genes determining the expression of those characters. The preferential mating of relatives, on the other hand will distort the distribution of all gene differences within the population, for the tendency of relatives to resemble one another arises from their community of ancestry and hence applies to all the genes they carry. The consequence of such inbreeding is progressively to increase the proportion of pure-breeding genotypes in respect of all gene differences, and if it is close enough and continued long enough this approach towards the pure breeding condition, or homozygosity as it is termed, is complete. Indeed this is the way in which homozygous or true-breeding lines are produced for agricultural purposes in other species of animals and plants. Now in normally out-breeding species such as man, the homozygous pure-breeding lines are characterised by a general debility, a lack of vigour, of fertility and of resistance of inclement conditions and disease. This inbreeding depression sets in when inbreeding commences and increases as the inbreeding progresses and the proportion of genes in the homozygous condition rises. We have no direct evidence of gross inbreeding depression in man, because we have no observations of a human lineage in which close inbreeding has gone on generation after generation. We do, however, have evidence of some increase in both disability and disease among the offspring of cousin marriages and we can hardly doubt that inbreeding depression would be displayed in just the same way by man as by other species of similar genetical properties.

It is significant therefore that inbreeding is controlled in one way or another in all human communities, even the most primitive. The Australian aborigines for example have their system of distributing the members of the tribe into "lineages," mating being allowed only between certain lineages in such a way as to preclude the union of close relatives. In Western Christendom the prohibited degrees of marriage serve the same purpose. Union of the genetically closest kinds, between parent and offspring or brother and sister, are completely prohibited. Those of the next closest kind are almost entirely proscribed; for grandparent and grandchild may not mate, nor usually uncle and niece or aunt and nephew; but the marriage of double first cousins, who are genetically as similar, is permitted. The double first cousin relationship is however a rare one and the frequency of marriage between double first cousins is so low as to have no significant consequences for the population. The marriage of ordinary first cousins is, of course, not uncommon, but here the genetical relationship is not very close and, though detectable, the consequences of this mild inbreeding are generally not serious. Perhaps the most noteworthy of them is a greater likelihood of certain types of genetical abnormality turning up in the offspring of first cousins than in the offspring of the general run of marriages within the community.

Devices for the control of inbreeding are not confined to man. They are in fact a commonplace of out-breeding species in plants as well as animals. It is from the study of their effects and of the experimentally enforced circumvention of their action in these other species that we can understand the significance of the ban on incestuous unions in man himself. Man is, however, unique in his way of controlling inbreeding, for he achieves it by the promulgation of communal laws and their enforcement through communal action—a system which is obviously not available to other species. We shall return in a later chapter to consider this matter further in another of its aspects.

4

Mutation and Selection : Radiation and Medicine

Mutation

Even within a population where mating is effectively at random the simple Hardy-Weinberg proportions may be upset by changes in the relative frequencies of the alternative genes *N* and *A*. These upsets may themselves be produced by two agencies, mutation and selection. Mutation is simply the change of one gene into another, of *N* into *A* or, of course, in principle of *A* into *N* also. As we have seen, however, most mutations of the kind we are concerned with result in a reduction of the efficiency with which the gene produces its effect or even in a complete loss of the capacity to do this work. Thus, for example, the liver of a normal person contains an enzyme which catalyses the conversion of one amino-acid, phenylalanine, into another, tyrosine. This enzyme is missing from individuals suffering from the disease phenylketonuria who therefore cannot convert phenylalanine into tyrosine. Now like all amino-acids, both phenylalanine and tyrosine play their part as building blocks in the manufacture of proteins, each of which has a specificity depending on the amounts of the various amino-acids it contains and the arrangement of these amino-acids in its structure. The loss of the capacity to convert one amino-acid into another is thus bound to upset the balance among the different kinds of proteins that an individual manufactures in his cells. Furthermore, to the extent that tyrosine, and consequently the proteins that contain it, are in short supply, phenylalanine will be present in excess. Not all of this excess is used in protein manufacture and indeed a great deal of it is converted into, among other things, a substance known as

phenylpyruvic acid which is not an amino-acid to be used in protein manufacture and is in fact excreted in the urine. It is the presence of this substance in the urine by which the condition is diagnosed and from which it derives its name of phenylketonuria, phenylpyruvic acid being in fact one of the type of substances known as ketones.

Just how this biochemical upset produces the mental deficiency characteristically associated with it is not yet known with certainty, but it is thought to be because the substances into which the excess phenylalanine is converted interfere with the proper development of the cells in the brain during the first two years of life. Be this as it may, there is the obvious possibility that if the excess of phenylalanine can be removed by feeding a diet low in its content of this substance, the biochemical upsets could be reduced. The necessary tyrosine of course also must be provided in the diet. Attempts to remedy the condition in this way have given promising results. Obviously if the disturbance to the proper development of the brain cells occurs in very early life the condition must be recognised and the diet adjusted with a minimum of delay after birth. The simple test necessary for recognition is therefore now being applied to the urine of all babies born for example in Birmingham and the West Midlands conurbation. About one baby in twenty thousand is a phenylketonuric and reacts to the test, and up to three cases a year are discovered in this way in this part of England.

The phenylketonuric condition arises because of the failure of a normal biochemical process and its treatment depends on rendering this process unnecessary. Genetically the affected individuals differ from normal in one gene, being in our notation *AA*. *NA* individuals do not display the condition though they do show a slight departure from the normal biochemical pattern. The gene *A* is evidently incapable of mediating the production of the enzyme which catalyses the conversion of phenylalanine to tyrosine, an enzyme for whose production the normal gene *N* is responsible. Thus the process of mutation by which *A* arose, and presumably continues to arise from *N*, resulted in a loss of function and so may be regarded as a process of degeneration. In principle we must suppose that *A* could

change back to *N* and regain its function, but it might well be expected that change would be much more likely to reduce the efficiency of working of a finely adjusted piece of machinery like a normal gene than to restore adjustment and full function to one that has broken down. It is not surprising therefore that even in species so well studied as the fruit fly, *Drosophila melanogaster*, there is little reliable evidence of the back mutation to normal of genes which have themselves arisen by mutation from the normal. We may thus reasonably regard the process of mutation, in the relation we have been discussing it, as effectively a one way process, at least to a first approximation.

Selection

Mutation is a rare event: experience from other species suggests that one germ cell in a hundred thousand or a million or even more may carry any given gene in a newly mutated form and such evidence as we have from man is in agreement. Nevertheless, if *N* was steadily mutating to *A* without any change in the reverse direction, *N* would vanish over the generations and we should all become *AA*. Even if *A* occasionally changed back to normal, it would still be more common than *N* provided this reverse mutation was less frequent than the forward change. Yet in point of fact, these abnormal conditions like phenylketonuria, haemophilia and achondroplasia are rare. The reason is that they are unfitting to the individuals who display them: these individuals leave fewer progeny than normal, or even none at all, so that they contribute fewer genes to later generations. The condition, and with it the gene from which it arises, is thus being acted against by natural selection. Furthermore in tending to reduce the mutant gene *A* in the population, selection is opposing the mutation whose effect is to raise the frequency of *A* at the expense of *N*. Where will the balance be struck between them?

The best documented case to consider is achondroplasia. This dwarf condition is due to a single gene difference from normal, and the effects of gene change is such that the dwarfism is displayed by individuals (described as heterozygotes) who carry only one mutant gene together with a normal gene, i.e. individuals who are *NA* in constitution. Such a mutant gene

is said to be dominant over normal, in contrast to recessive mutant genes which produce their characteristic effects only when in the homozygous, *AA*, condition, *NA* individuals resembling the normal *NN* in character. The gene for phenylketonuria is generally, and conveniently, regarded as recessive though this is something of an over-simplification since, as we have seen, individuals carrying only one phenylketonuria gene together with a normal counterpart are distinguishable from fully normals by an appropriate biochemical test, albeit they display none of the gross abnormality of a phenylketonuric.

Now, the achondroplasia gene being dominant, any individual carrying it will display its effects. So any achondroplasiac individual receiving the gene by hereditary transmission must have at least one achondroplasiac parent. If neither parent is achondroplasiac the gene displaying itself by achondroplasia in the offspring must be newly arisen by mutation from its normal counterpart. It has been recorded by Mørch,[23] who traced all the achondroplasiac dwarves in Denmark, that out of 94,075 children in certain Copenhagen maternity records 10 were achondroplasiacs. Of these 10 only 2 had an achondroplasiac parent so that 8 must be regarded as carrying newly mutated genes. Since each child carries two genes and only one of these would be a new mutant in each of the eight children we can see that 8 out of $2 \times 94{,}075$ genes, i.e. approximately 8/188,000, had undergone mutation. Thus each normal gene has a chance of 8/188,000 or 43 in a million of mutating in each generation. This is normally expressed by saying that the mutation rate, μ, of the gene is 43/1,000,000.

Turning to fitness, the 108 dwarves that Mørch traced had only 27 children between them, whereas their 457 normal brothers and sisters, who provide the best control comparison, had 582 children. Thus on the average each dwarf left only $\frac{27}{108} = 0{\cdot}25$ children whereas each normal left $\frac{582}{457} = 1{\cdot}27$ children. The dwarves produced only $\frac{0{\cdot}25}{1{\cdot}27} = 0{\cdot}2$ of the children their brothers and sisters contributed to the next generation. To put it another way the achondroplasia gene reproduces itself at

only 0·2 of the rate of its normal counterpart. It is as though 0·8 of the achondroplasia genes were being eliminated in every generation—which is exactly balanced by 8 out of 10 of the genes being new mutations. This exactness of balance, however, should not be given too much weight as figures of this kind are subject to statistical variation. Indeed of the 27 children of dwarves only 10 were themselves dwarf, instead of the $\frac{1}{2} \times 27 = 13{\cdot}5$ which is the simple genetical expectation. This shortfall of dwarves in comparison with simple expectation may itself be due merely to statistical fluctuation, or on the other hand it may indicate an even greater handicap than our calculation suggests. However this may be, clearly selection and mutation are in at least approximate balance.

With the aid of a little mathematics we can probe further into the situation. Let us go back to the Hardy-Weinberg rule. With u as the proportion of normal genes (N) and v ($=1-u$) the proportion of achondroplasia genes (A) the proportions of the types in the population will be:

Genotype	NN	NA	AA
Phenotype . . .	normal	achondroplasiac	unknown
Proportion in population	u^2	$2uv$	v^2
Fitness . . .	1	$1-s$	$1-t$

Let the fitness of the normals (NN) be taken as unity, and that of the achondroplasiac (NA) be $1-s$; that is, let the achondroplasiacs on the average leave only $1-s$ children for every 1 left by the normals. We do not know what the fitness of AA individuals would be, or what character they would display or even whether their two A genes would make them so grossly abnormal that they could not survive. Since, however, only 10 of our nearly 200,000 genes in the Copenhagen babies were A, v must be only the order of 1 in 20,000 so that v^2 would be 1 in $20{,}000^2$, i.e. 1 in 400,000,000, which is so small as to be safely neglected. So it does not really matter what the

properties of AA individuals are. We will nevertheless set their relative fitness at $1-t$ for the moment.

The proportions of the two types of genes are $u:v$ in the germ cells from which the individuals arose. Normal genes will be passed on to all the germ cells of NN individuals and to half the germ cells of NA individuals, which would give us $u^2+\frac{1}{2}(2uv) = u$, if NA left as many children as NN. But NA leaves only $1-s$ as many children so we have $u^2+uv(1-s)$ as the N bearing germ cells produced by this generation. Similarly there will be $uv(1-s)+v^2(1-t)$ germ cells bearing A genes. The figures, however take no account of mutation, which will in fact ensure that a proportion μ of the N genes (themselves constituting a proportion u of the population) change to A. The ratio of N to A genes in the germ cells will thus be $u^2+uv(1-s)-u\mu$: $uv(1-s)+v^2(1-t)+u\mu$. Thus with a little algebraic manipulation we see that the proportion of germ cells carrying N genes will be $\frac{u(u+v)-uvs-u\mu}{u^2+2uv+v^2-2uvs-v^2t}$ which because $u+v=1$ can be rewritten as $\frac{u-uvs-u\mu}{1-2uvs-v^2t}$, where the denominator is of course the total number of germ cells, whether carrying N or A. If the population is in equilibrium this proportion must equal u, the proportion of N genes in the germ cells produced by the previous generation and from which this generation of individuals is derived. So, for equilibrium, we can set $\frac{u-uvs-u\mu}{1-2uvs-v^2t} = u$. Dividing both sides by u gives $\frac{1-vs-\mu}{1-2uvs-v^2t} = 1$, which we can rewrite as $1-vs-\mu = 1-2uvs-v^2t$. Now v^2 is so small as to be negligible so that we can forget the term v^2t on the right of the equation. Similarly u is very nearly 1 so that we can put $2vs$ as a reasonable approximation for $2uvs$. Our equation then becomes $1-vs-\mu = 1-2vs$ which simplifies to $sv = \mu$ or $v = \frac{\mu}{s}$.

The proportion of achondroplasiacs in the population is $2uv$ which, with u so nearly 1, is virtually the same as $2v$, so that if we write f for the proportion of affected individuals

$$f = 2v = \frac{2\mu}{s}.$$

The proportion of affected individuals at equilibrium in the population thus increases in direct relation as the mutation rate rises and falls directly as the unfitting effect of the gene gets larger.

Do the Danish observations on achondroplasia agree with this relation? The maternity records show that 10 children were achondroplasiac out of 94,075, so that we can estimate the proportion of affected at birth as $f = \frac{10}{94{,}075} = \frac{106}{1{,}000{,}000}$ or 106 in every million. We have already found the mutation rate to be $\frac{43}{1{,}000{,}000}$ and the fitness, $1-s$ to be 0·2, so that s, the unfitting effect of the gene, is 0·8.

So $\frac{2\mu}{s} = \frac{43 \times 2}{1{,}000{,}000 \times 0{\cdot}8} = \frac{108}{1{,}000{,}000}$ which agrees very closely with the value observed directly for f.

We have already had occasion to note that our estimates of the various quantities are subject to statistical variation. The extreme closeness of the agreement must not therefore be given too much weight. It is clear, however, that there is no reason to doubt the adequacy of our interpretation of achondroplasia in Denmark in terms of a balance between mutation rate and natural selection, or that these forces have come to equilibrium in the Danish population. For every new A gene arising by mutation, one is lost through the action of natural selection (Fig. 6).

This simple type of equlibrium relation between f, μ and s is not confined to dominant genes like achondroplasia. If we consider a recessive gene the situation may be set out as:

Genotype	NN	NA	AA
Phenotype	normal		affected
Proportion of population	u^2	$2uv$	v^2
Fitness	1	1	$1-s$

and a calculation similar to that carried out for dominant genes yields $f = v^2 = \frac{\mu}{s}$ at equilibrium. There is now no factor of 2 in the numerator of the fraction, but the proportion of afflicted individuals goes up with the mutation rate and down with the unfitting effect of the genes just as before. The same general rule applies also if the fitness of the heterozygous, NA, individuals is intermediate between the fitness of NN and AA.

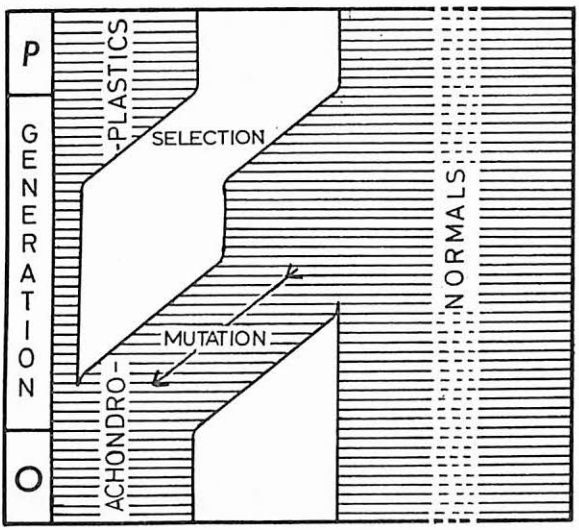

FIG. 6. Balance of mutation and selection in achondroplasia. Selection reduces the proportion of achondroplasia genes relative to their normal alternatives by 80 per cent in each generation. New achondroplasia genes arise by mutation from the normals. When the incidence of the abnormality is at equilibrium in the population the loss by selection is exactly replaced by the gain from mutation. *P* indicates the parental generation and *O* the offspring.

Mutation rates are in general low—of the order of one in a hundred thousand or one in a million or even lower. Unless, therefore, the unfitting effect of the mutant gene is also very small, so that the individuals displaying the gene's effects are very nearly as fit as normals, we must expect the proportion

of afflicted people in the population to be small. In the extreme case where the afflicted leave no children, so that their fitness is zero and $s = 1$, the proportion of afflicted will at most be only twice the mutation rate, with a dominant gene, and no higher than the mutation rate itself with a recessive. Where the condition the gene determines is at all common in a population we must always suspect that the situation does not depend on a balance between mutation and selection, but that the balance is of a different kind which we shall examine in the next chapter.

We should expect that the general relationship between f, μ and s would be of wide application, wherever in fact the proportion of the population displaying a genetically determined abnormality is low. Many abnormalities do come into this class. Even chromosome upsets such as that which produces mongoloid idiocy can be treated like dominant gene changes for this purpose. We seldom, however, have evidence about them comparable to that for achondroplasia. So we can seldom be quite sure that interpretation in terms of a balance between mutation and selection is valid. Success in understanding achondroplasia was made possible only by extensive and detailed studies of this condition in a suitable population. Furthermore, the mutation rate was relatively easy to measure since, being dominant, the achondroplasia gene displays its effects in virtually every individual carrying it. The measurement of mutation rates for recessive genes, on the other hand, is troublesome even in the majority of plant and animal species with which we experiment, and estimates of the mutation rates to recessive genes in man is impossible to obtain by direct means. Nor is the estimation of s, the degree of unfitness, always easy (see Clarke [8]) for this not only involves comparisons with normals, who obviously must be taken so as to provide an informative comparison, but should also be based on the average number of children left by each affected individual who is born, not merely by those who survive to maturity and marriage: obviously fitness may be reduced by failure to survive as well as by failure to reproduce. Finally even the estimation of the number of individuals affected by a condition in a population can pose its problems. Some of these are

statistical in nature, but others are biological as for example when individuals die before the age of onset of a condition which appears only in later life. In the absence of precise information however, we probably do not fall into great error if we adopt as a working assumption that rare genetical conditions are held in the population by the balance of mutation and selection.

Upsetting the Balance

It is obvious from the relation between the proportion of affected individuals, f, the mutation rate, μ, and the unfitting effect of the gene, s, that the balance can be upset both by changing μ and by changing s. The mutation rate can be raised by subjecting the genetic materials to ionising radiations and to a wide range of chemical substances. At present we know of no means of reducing the rate of mutation. Since at equilibrium the proportion of affected individuals goes up directly with the mutation rate, this means that we can raise the number of afflicted people in later generations but not lower it, at least by using any of our present means of manipulating the mutation process. The mutagenic effects of ionising radiations have been known since 1927, but only during the past few years has it become a matter of public interest, largely because of concern expressed about the genetical effects of radioactive fall-out from bomb tests.

How serious are the genetical hazards to man of ionising radiations? In seeking an answer we must ask two further questions. How widespread in a population such as our own are genetically determined abnormalities of the kind with which we are concerned? And to what extent are we raising mutation rates by present levels of exposure to man-made radiations? Both questions are capable of answer only in general terms. To answer the first it is not sufficient to count the individuals affected by abnormalities whose genetical determination is known with certainty, for in our present state of knowledge this must be a gross underestimate. We must include the best allowance we can make for conditions suspected of genetical determination, bearing in mind that some conditions arise at times from genetic and at others from environmental

causes, and that still other conditions may depend on an interaction between particular genotypes and particular environments, as where for example a mental upset results in an individual of a special genotype who has become exposed to a special environmental stress. Stevenson [34] has concluded from studies of the Northern Irish population that some 4 per cent of individuals born are subject to long-term handicaps of one kind or another, anatomical, physiological or mental, and that at least one-quarter of these owe their condition to specific mutant genes. Applying these proportions to a population of 50 millions, such as we have in the United Kingdom, at least 500,000 people are afflicted in some gross way or other as a result of the genes they carry. Carter [6] has carried out a detailed study which yields essentially the same conclusions as Stevenson's. Omitting upsets due to the extreme expression of continuous variation and confining attention to discrete conditions, he concludes that in our population of 50 millions there must be nearly 600,000 individuals displaying a range of disabilities of all kinds, anatomical, mental and physiological, for specific genetical reasons.

This total of the genetically handicapped somewhat exceeds the estimated number in hospital in Great Britain, though of course the two groups, while overlapping, do not coincide since many are in hospital for other than genetical handicaps and many of the handicapped are cared for at home. The similarity of the numbers, however, gives an idea of the load which genetical handicap imposes on the population of this country. The problem of genetical handicap is clearly not one to be lightly dismissed.

Assuming that all the genes mediating these conditions are held in the population at their characteristic frequencies by the balance of mutation and selection, a permanent doubling of the mutation rate would mean a doubling of the proportion of the handicapped in the long run when equilibrium had again been reached. To what extent, however, are present practices raising the mutation rate? Clearly only radiation reaching the reproductive organs of individuals during or prior to reproductive life can have an effect on later generations. This means that we are concerned on the average with only the first 30

years of life, since the average age of parent at the birth of a child is about 30 years in men and slightly lower in women. During this period each of us receives about 3 rads of so-called background radiation, that is radiation from natural sources, especially the rocks and similar materials around us and cosmic rays from space. The amount of radiation received varies with the composition of natural background, people living in areas where there is a lot of granite receiving up to twice as high doses as those in other areas.

Now if all our spontaneous mutations were an effect of this background radiation the addition of an average dose of 3 rads per individual would double the mutation rate. It is, however, very unlikely that all, or even the majority, of our spontaneous mutations are traceable to natural radiations and while we do not know with any precision the average dose of radiation required to double our mutation rate there is some indication that it may well be more like 30 rads per individual. We will adopt this value as the best available. This would imply that about one-tenth of our spontaneous mutations are traceable to the action of natural radiation.

The average genetically effective exposure to man-made radiation of the population in Great Britain is also not known with full precision. A reasonable estimate would seem to be about 3 rads at most [21 22]. This is traceable very largely to the exposure of patients to radiation for the purposes of medical diagnosis and treatment. Small contributions, each of the order of one or two per cent of the total, are made by exposure to the radioactive materials of luminous watches and clocks and by exposure of the radiological staff in hospitals and industry. The contribution from the fall-out of nuclear weapon tests varies with the amount of testing undertaken. A few years ago it was no higher than that from luminous watches and clocks, but it must have risen recently. Even now, however, it cannot be more than a few per cent of the total, and therefore small by comparison with the contribution from medical practices. It should decline again now that testing has been restricted by treaty.

Taking the doubling dose as 30 rads and the average exposure to man-made radiation at 3 rads, we are raising the mutation

rate by 10 per cent of its spontaneous value. So if the present levels of exposure are continued until a new equilibrium is reached between mutation and selection in the population we would expect a 10 per cent increase in the numbers of genetically handicapped. This would amount to some 50,000-60,000 additional handicapped individuals in our population of 50 millions (of which however only some 1000 or 2000 would be ascribable to the effects of fall-out). Such an additional load of handicap and suffering is clearly not to be taken lightly and everything reasonably practicable should be done to reduce it by reducing exposure to the radiations. In fact, statutory requirements and codes of practice covering places where radiations are used in industry, medicine and research, are now being introduced, partly to the end of controlling genetic handicap in future generations and partly to control the more immediate hazard of harm to the individuals actually receiving the radiation. At the same time we must bear in mind that benefit is derived from the use of radiations in industry and, especially, medicine. Indeed it is difficult to see how medicine as we know it would be possible without the use of radiations. The benefits must weight heavily in the balance against the harm radiation does. No one would think of abandoning road transport or heating devices in houses because of the accidents that result, though of course, we must always be striving to minimise these ill consequences. The same principles should govern our attitude to most of the practices requiring the use of radiations.

A permanent increase in the mutation rate will mean a corresponding rise in the affected and handicapped proportion of the population when the new equilibrium is reached. So also will a reduction of the value of s, the unfitting effect of the gene on those manifesting its consequences, and the effective medical treatment of genetical disabilities must in general be expected to bring about such a reduction. To take an example, before Banting and Best discovered how to treat diabetes melitus by supplying insulin artificially, the unfitting effect of this decrease was almost complete: s was almost 1. Even now the fertility of diabetics is by no means as high as that of their normal fellows, but it has been raised materially. Such evidence as we

have suggest that it would not be unreasonable to assume that it is now about one-third of the normal, so that s now has a value of about two-thirds. The old equilibrium would thus be struck at $\frac{\mu}{1}$ and the new one (assuming s to stay constant until equilibrium is reached) at $\frac{\mu}{\frac{2}{3}}$. This means a rise of 50 per cent in the numbers born into the population suffering from this form of diabetes. The increase in a population such as our own would in fact be greater than this because not only would more diabetics be born, but they would on the average live longer. Indeed in the years between 1927 and 1946, the number of people suffering from diabetes mellitus recorded in Denmark rose to more than three times its original level,[1] and this must be due almost entirely to non-genetic causes, for twenty years is far too short a time for the new genic equilibrium even to be approached. Nevertheless the upset of genic equilibrium must add its quota in the long run.

The effect of treatment is clearer with pyloric stenosis. In this condition an obstruction present in the pyloric region of the stomach leads to fatal results very early in life if untreated, though here the genetical basis of the condition has yet to be worked out in detail. Carter [5] records that the incidence of this condition in the population is about 5 per thousand among male infants and about 1 per thousand among females. A surgical treatment was introduced some forty years ago and observation of the offspring of successfully treated individuals are now coming available. Carter has found 11 affected among 162 sons and 2 affected among 161 daughters of treated males, and 9 affected among 44 sons and 4 affected among 36 daughters of treated females. These are very great increases over the levels within the general population, so that whatever the details of the genetical determination may be, the genes responsible must be increasing in frequency as a result of the treatment.

The effective treatment of genetically determined conditions of the kind we are discussing must in the long run raise the incidence of those conditions. This is obviously in no sense an argument for denying treatment: indeed it may well be held that the rise in incidence of a disability is not to be taken as a

cause of undue concern where an effective treatment not only exists but is itself the cause of the raised incidence. This argument itself on the other hand is valid only within limits, since any rise in disability, even treatable disability, increases the load that society must bear in providing the treatment and general medical care. To recognise that such limits must presumably exist to this argument is, however, at present no more than an academic exercise, since there are but few genetically determined disabilities which we can treat by external intervention.

One of the most striking medical changes in the past century has been the virtual elimination of a number of infectious diseases by improving hygiene and sanitation. That we have genes for resistance to such diseases can hardly be in doubt: similar genes are a commonplace in other species and we have evidence of a genetic element in resistance and susceptibility in tuberculosis (Fig. 2). With the elimination of an infective disease individuals carrying genetical resistance to it would lose the advantage they formerly enjoyed over their fellows. The genes responsible for resistance could then hardly fail to diminish in frequency in the population, though the diminution could in no way be regarded as raising any serious problems since no one would in any case willingly contemplate a return to the environmental conditions of the past. That such a change has occured is, of course, entirely surmise, for again we do not have the evidence needed to establish the present genetical situation in our population, and still less the evidence about the genetical situation as it was. It is, however, known that populations may lack almost completely any resistance, whether of genetic or other origin, to infective disease to which they have not been exposed. The consequences of the disease when it is introduced into such a population can of course be devastating by comparison with its effects in a population accustomed to it and therefore presumably carrying resistance to it.

Re-striking the Balance

Where the mutant gene is dominant, as with achondroplasia, each new mutation displays its effects at once in the first

individual to receive it. The full consequences of raising the mutation thus quickly become apparent, and the greater the unfitting effect of the gene the more quickly the consequences are displayed. In the case of achondroplasia, the reduction in fitness is 4/5 and at equilibrium 4/5 of the achondroplasiacs in the population are due to new mutations. Under the existing equilibrium in Denmark there appears to be about 106 affected individuals in each million births. For ease of calculation let us round this off to 100 of which 80 are due to new mutation and 20 to transmission of the gene from a parent. If the mutation rate is doubled, the next generation will contain $80 \times 2 = 160$ per million achondroplasiacs owing their condition to new mutation, but still only 20 owing it to transmission from a parent, giving a total of 180. These will contribute $\frac{1}{5} \times 180 = 36$ cases by transmission to the second generation which, if the doubled mutation rate persists, will again carry 160 mutational cases making 196 in all. The third generation will similarly carry $\frac{1}{5} \times 196 + 160 = 199{\cdot}2$ cases, and the fourth generation $\frac{1}{5} \times 199{\cdot}2 + 160 = 199{\cdot}84$ so that the new equilibrium with a doubled proportion of achondroplastics is virtually established in only the fourth generation. In man this is just over a century if we take the generation time as about 30 years.

The fall in the number of cases is equally rapid if the mutation rate is lowered again. Suppose the mutation is doubled for one generation only. The incidence in that generation's offspring is 180, but with the return to the original mutation rate the second generation will contain only 80 mutational cases to which are added $\frac{1}{5} \times 180 = 36$ cases due to transmission or 116 in all. The figure for the third generation will be $80 + \frac{1}{5} \times 116 = 103{\cdot}2$ and for the fourth $80 + \frac{1}{5} \times 103{\cdot}2 = 100{\cdot}64$ and the incidence is back virtually to the original value.

The consequences of lowering the unfitting effect of the gene

can be worked out in the same way. Suppose the unfitting effect is halved, s being reduced from $\frac{4}{5}$ to $\frac{2}{5}$ with the consequence that $\frac{3}{5}$ of the genes present in one generation are transmitted to the next. Starting with an incidence of 100 per million,

Speed of changes in approximate numbers of achondroplasiacs per million when the mutation rate and the level of unfitness are altered.

Generation	Mutation rate doubled		Unfitness halved	
	Permanently	For one generation	Permanently	For one generation
Initial	100	100	100	100
after change 1	180	180	140	140
2	196	116	164	108
3	199·2	103·2	178	102
4	199·8	100·6	187	100·3
9	200·0	100·0	199·3	100·0
Ultimate	200	100	200	100

By contrast: in 9 generations following a permanent doubling of the mutation rate the incidence of phenylketonuria would increase by less than 9 per cent, i.e. there would be rather less than 109 cases for every 100 in the initial population.

and holding the mutation rate constant, the first generation to feel the effect of the change in fitness will carry 80 cases due to new mutation and $\frac{3}{5} \times 100 = 60$ due to transmission or 140 in all. The second generation will contain $80 + \frac{3}{5} \times 140 = 164$, the third $80 + \frac{3}{5} \times 164 = 178{\cdot}4$, the fourth $80 + \frac{3}{5} \times 178{\cdot}4 = 187{\cdot}04$

and so on, with the doubled incidence of new equilibrium being virtually attained by the ninth generation (that is in a little short of three centuries) when the incidence will have risen to 199 per million. The consequences of changing the unfitting effect of the gene are less quickly realised than those of altering the mutation rate but they are nevertheless fairly rapid in terms of generations.

The situation with recessive genes, like that for phenylketonuria, is very different. Being recessive the newly mutant gene does not display its effects in its first carrier who will be *NA* in constitution, apart from the unlikely event of the individual producing the mutation being married to one of the *NA* individuals already existing in the population, and the two *A* genes (one new and one old) coming together in the offspring. In the same way the first individual carrying the new *A* gene is most likely to mate with an *NN* normal so that the *A* gene is again passed on undetected by its effect because concealed under the cloak of its recessiveness. So only a few of the *A* genes carried by a population will be displaying their effects in *AA* individuals and only this few will be exposed to elimination by the selection arising from their unfitting effect on the *AA* people. The gene will in fact be vastly more common than the condition (which as we have seen, is displayed by only v^2 of individuals where v is the frequency of the gene) and the proportionate addition made by a raised mutation rate to the pool of concealed *A* genes will be correspondingly small. Penrose [28] estimates that whereas, at equilibrium, 4 out of 5 achondroplasiacs are due to fresh mutation, only 1 out of each 100 phenylketonurics are ascribable to it. Even though the unfitting effect of phenylketonuria is complete, a repetition of the calculation used above for achondroplasia, will show that permanently doubling the mutation rate adds only 1 per cent to the incidence in the first generation, a further 0·99 per cent accruing in the second generation, 0·98 per cent in the third and so on. Over fifty generations (that is more than 1500 years in man) would be required to move half way to the new equilibrium, or in other words, to raise the existing incidence of the condition by half. Only after a tremendously long period would this new equilibrium be approached, with the doubled

incidence of phenylketonuria. The consequences of permanently halving the unfitting effect of the gene, while ultimately leading to the same doubling of the incidence of the gene, would give an even slower approach to this new equilibrium.

The reverse side of the penny is, of course, that any fall in the incidence towards a lower equilibrium would be equally slow. If the mutation rate of the achondroplasia gene were doubled for one generation only there would be an immediate rise of 80 per cent in the incidence of the condition followed, as we have seen, by a rapid fall with the original incidence virtually regained after another four generations. With phenylketonuria the initial rise would be only 1 per cent, but the subsequent fall would be so slow as to be hardly detectable over the next five generations and it would be a very long time before the original low incidence were regained. The reason for the slow fall in incidence of the condition is the same as that for its slow rise when the mutation rate is raised: whether pre-existing or newly mutated, all but a very small fraction of the mutant genes lie hidden behind their recessiveness in the heterozygous, *NA*, individuals. The homozygous, *AA*, individuals who display the condition in fact carry only a fraction of the *A* genes—in phenylketonuria only about 1 in 200 of them. The remaining 99·5 per cent are concealed. Nevertheless they are there and they will emerge gradually yet inexorably to express their efforts by giving rise to phenylketonuria when *NA* mates with *NA* and produce *AA* individuals as one-quarter of their progeny. The consequences of a raised mutation rate may unfold themselves very slowly. The newly mutated gene may take centuries or millenia before it expresses itself by playing its part in the production of a phenylketonuric. But eventually it will produce its effect, and the suffering that a mutant gene can cause is not any the less because the mutation occurred a hundred years ago or a thousand. We hold our genes in trust for our descendants as our ancestors held them in trust for us, and it is a trust to which there is no foreseeable end.

Before leaving this subject of genes held in the population by the balance of mutation and selection, we may perhaps

pause for a moment to look at the effects that might be expected from the eugenical programmes that have been advocated from time to time, based on "sterilisation of the unfit." Now sterilising phenylketonurics would clearly have no effect, for as it is they leave no progeny, and sterilising all achondroplasiacs would reduce the incidence in the population only by 20 per cent since even now 80 per cent of the genes are lost in each generation because of the reduced fitness (in the sense we have been using the term) of the carriers. But unfitness as eugenists use the terms means social unfitness, which is not tied to biological or Darwinian unfitness of the kind we have been measuring by *s*. A gene which produced social unfitness without lowering biological fitness could be reduced in frequency by sterilisation of those displaying its effects, though obviously not below the value at which it would be held in the population by mutation, and if the gene were dominant the reduction could be rapid. If, however, the gene were recessive the reduction in incidence of the condition would, as we have seen, be inordinately slow.

Now our knowledge of human genes and their mutation is insufficient to tell us how many of those conditions the eugenist might be seeking to remove would arise from dominant genes and how many from recessive genes. Our experience from species like the fruit fly, *Drosophila*, suggests that the recessives might be much the more numerous, perhaps even ten times as many as the dominants. So even leaving aside the difficulty of agreeing general criteria for deciding what, for this purpose, constituted social unfitness, a sterilisation programme could barely dent the problem.

Other more promising, and to most people less repugnant, approaches are available. If couples having a child displaying an upset traceable to a recessive gene were to have no further children, the incidence of the disability in the population would be reduced; and it is found in practice by at least one Genetics Clinic that many couples do in fact curtail their families after the birth of an affected offspring. The reduction in incidence of the disability achievable by this policy is, however, necessarily limited because recognition of the parents carrying the gene depends on their producing an affected

child. A more drastic but prospectively more effective approach would be to seek out in each generation the *NA* individuals carrying a recessive gene but, of course, not displaying its ill effects, and endeavour to ensure that they did not marry others of the same constitution. All *NA* individuals would then have *NN* mates and since children must receive a gene from each parent, no *AA* child could arise except in the rate event of a mutation to *A* occurring in the *NN* parent. The gene would exist with unreduced frequency in the population, in fact with a slowly increasing frequency, but it would display its effects in an *AA* individual only extremely rarely.

The result would be achieved not by seeking to change the gene frequency but by adjustment of the systems of mating, which would no longer be random in respect of *NA* people. The interference with freedom of choice would not, however, be serious since, for example, the phenylketonuria gene is carried by only about one in a hundred of normal people so that only one prospective mate in a hundred would be ruled out. The difficulty in this approach to the control of the production of handicapped individuals by recessive genes lies in the need for discovering ways of detecting the prospective parents who are likely to be carriers, of type *NA*. Family relationships could be of great help where the condition has been known to occur, and in some cases mild symptoms or, as with phenylketonuria, biochemical tests could be used finally to distinguish the carrier members of the family from the normal. It is likely too, that we shall come to be able to recognise the carriers of further deleterious recessive genes by their biochemical characteristics. The difficulty of this approach to the control of genetical handicap is obviously not to be underestimated but it is not as great as might appear at first sight. Whether, however, in the case of any given genetic disability the attempt should be regarded as justified by any reduction it might be expected to achieve in the load that that genetical handicap lays on the individual, on his family, and on society itself, is a question whose answer must be based on social as well as genetical considerations. It is one which must, therefore, be decided by society as a whole.

5

Polymorphisms: Blood Characters

Sickle-cell Anaemia

When a gene is held in the population by the pressure of mutation the fraction of the population that displays its effect is small—about 1 in 10,000 with achondroplasia and 1 in 40,000 for phenylketonuria, to refer to two upsets we have discussed at some length. Not all genetically determined abnormalities are, however, so rare. There is, for example, a disease known as sickle-cell anaemia [2, 3] to be seen among the native inhabitants of various parts of Africa, the Mediterranean basin and India. Under certain conditions the red blood cells of individuals suffering from this ailment undergo a sickle-like distortion and also break down so that they lose their haemoglobin. The result is anaemia, with associated vascular obstruction and secondary upsets to the liver and other vital organs. Most of those affected by the disease die in childhood.

Sickle-cell anaemia is determined by a single gene difference from normal, the anaemics being homozygous for the abnormal gene, that is they are AA in our notation. The unfitting effect of the gene is obviously great, and it has in fact been estimated that at most the anaemics leave only about one-quarter as many offspring as do other individuals. Yet in some African populations it appears that as many as 4 or 5 per cent of the children may be born with this condition. Now, if the gene were held in the population by mutation the relation $f = \frac{\mu}{s}$ would hold and with f, the proportion of afflicted in the population, at say 4 per cent and s, the unfitness, at three-quarters we should expect $\mu = sf = 0{\cdot}75 \times 0{\cdot}04 = 0{\cdot}03$ or three mutations in every hundred normal genes. This would be a fantastically

high mutation rate, about 1000 times as high as the rate of mutation to the achondroplasia and phenylketonuria genes. Furthermore, it is higher than direct observation of the sickle-cell condition itself would allow. Evidently the balance here is not between mutation and selection. Some other agency must be at work.

The primary effect of the sickle-cell gene is on the haemoglobin of the red blood cells. Haemoglobin is made up of two parts, the "haem" and the "globin," which latter is protein and like all proteins is made up of amino-acids. The sickle-gene results in one amino-acid, glutamic acid, being replaced by another, valine, at a particular place in the protein. This small substitution affects the electrical charge of the molecule with the result that the molecules tend to aggregate when they have become deoxygenated, and this brings about the upsets to the red blood cells and the vascular obstruction to which reference has already been made. The sickle-cell haemoglobin, in fact, is not sufficiently well adjusted to the essential function of oxygen transport in the body.

Now a heterozygous individual, carrying both the normal gene and the sickle-cell gene, that is an *NA* individual in our general notation, has both normal haemoglobin and sickle-cell haemoglobin in his red cells, there being rather less of the sickle-cell type than of the normal. The presence of rather more than half normal haemoglobin prevents the development of the abnormal behaviour in the red blood cells of the circulating blood so that the severe condition seen in the homozygous sickle-cell anaemics does not occur. These heterozygotes are thus like normals in that they do not suffer from the disadvantage of the homozygous sickle-cell anaemics, though they can be distinguished from the *NN* normals by the sickle-like distortion of their blood cells in appropriate tests. They are said to show the sickle-cell trait as opposed to the sickle-cell anaemia of the homozygous *AA* individuals.

The circulating blood of the heterozygotes behaves adequately in oxygen exchange because of the normal haemoglobin that it carries. At the same time the presence of the sickle-cell haemoglobin confers the unexpected advantage of resistance to malignant tertian malaria so that children displaying the sickle-cell

trait have a better chance of surviving the dangerous years of first exposure to the disease, before immunity has been built up, than do children without this character. The heterozygotes thus have an advantage over both types of homozygotes: because of their sickle-cell haemoglobin they have a resistance to malaria which is not shared by the homozygous normals, *NN*, lacking this haemoglobin; and because of their normal haemoglobin they avoid the anaemia of the homozygous sicklers, *AA*, who have nothing but the sickle-cell haemoglobin.

To see the consequences of this situation let us go back to the Hardy-Weinberg rule and see how it is modified by the opposing disadvantages of the normal and sickle-cell haemoglobins. The three genetic types and their properties are set out in the table below. As earlier, u is the proportion of normal genes and v $(= 1-u)$ that of sickle-cell genes in the germ cells of the population, but we now distinguish two unfitting effects, s_N in the *NN* individuals arising from lack of resistance to malaria and s_A in the *AA* individuals arising from their anaemia.

Genotype	*NN*	*NA*	*AA*
Phenotype	Normal Not resistant to malaria Not anaemic	Sickle-cell trait Resistant to malaria Not anaemic	Sickle-cell anaemia Resistant to malaria Anaemic
Proportion	u^2	$2uv$	v^2
Fitness	$1-s_N$	1	$1-s_A$

Now the germ cells effectively produced by this population will contain the N genes and A genes in the ratio $(1-s_N)u^2+uv$: $uv+(1-s_A)v^2$. At equilibrium this must equal the ratio $u:v$ shown by the germ cells of the previous generation so that we can write

$$\frac{(1-s_N)u^2+uv}{(1-s_A)v^2+uv} = \frac{u}{v}$$

which by a little simple algebraic manipulation reduces to

$$\frac{u(1-us_N)}{v(1-vs_N)} = \frac{u}{v}$$

giving $1-us_N = 1-vs_A$

or $us_N = vs_A$.

Thus at equilibrium the relative frequencies of the two genes in the population will depend on their relative disadvantages, the gene associated with the greater disadvantage being the rarer. Observation shows that the average expectation of progeny of each anaemic born is at most only one-quarter that of the individuals showing the sickle-cell trait. So $1-s_A = \frac{1}{4}$ and $s_A = \frac{3}{4}$. No information is available about s_N, the magnitude of the disadvantage that their greater susceptibility to malaria imposes on the normals, but this can obviously be calculated if we know the frequency of the sickle-cell character in the population and are prepared to assume that it is in equilibrium. The relation of s_N to the proportion of the surviving adult population showing the sickle-cell trait is shown in Fig. 7. The highest incidence of the sickle-cell trait among negro populations in Africa is some 40 per cent. As will be seen from the graph, this corresponds to a value of 0·2 for s_N, that is the fitness of the normals is reduced by malaria to 0·8 of that of the sickle-cell heterozygotes. With an incidence of 10 per cent for sickle-cell individuals in the population the disadvantage due to malaria is down to 0·04, and the less the disadvantage becomes the lower the incidence of the sickle-cell character. Now the disadvantage of *NN* individuals will depend on the risk of malaria, and where the population lives in an area free from malaria this risk is removed so that $s_N = 0$. The sickling gene will accordingly vanish too, or rather it will revert to the situation of the genes for achondroplasia and phenylketonuria and be held in the population only by the pressure of mutation. Sickle-cell anaemia will then, of course, be very rare, for the pressure of mutation is very low by comparison with the pressure of selection. Indeed it is for this reason that mutation has been ignored in our consideration of the equilibrium of the sickle-cell gene: when we are dealing with

equilibrium under opposing selective forces of the magnitude exerted by anaemia and malaria the effect of mutation is clearly negligible.

It would obviously be expected that the sickle-cell gene would be much commoner where malaria is being transmitted throughout the greater part of the year than where the disease is seasonal or present only in very restricted pockets, and the gene should be absent where the disease is absent. A survey made by Allison [2] of 35 tribes in East Africa shows this to be the case. The differences in frequency of the gene cut right across the lines of racial, linguistic and ethnographic difference, but follow well the patterns of incidence of malaria. Allison has also been able to show selection at work, by demonstrating that among infants prior to the age of mortality from anaemia

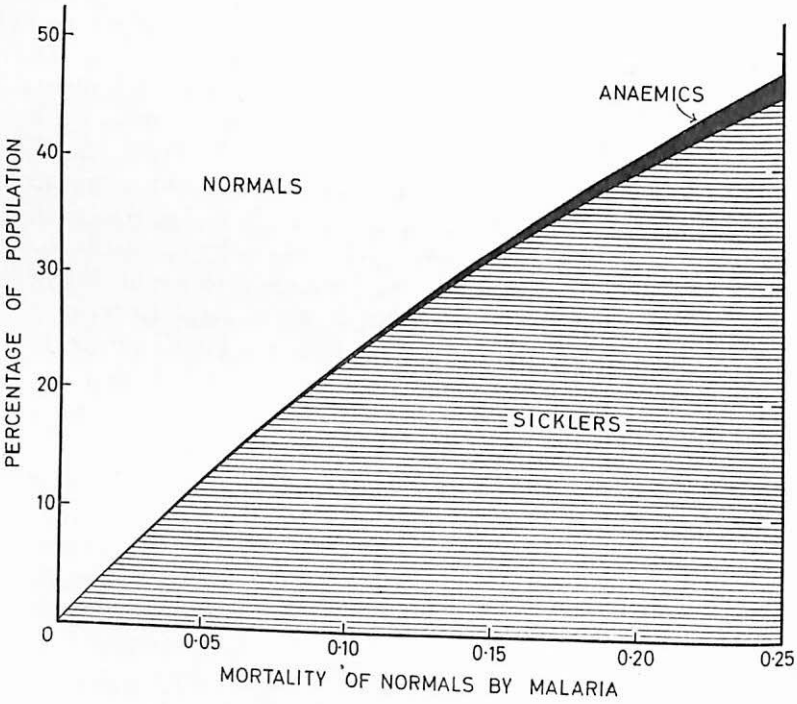

FIG. 7. The proportions of normal (*NN*), sicklers (*NA*) and sickle-cell anaemics (*AA*) in a population at equilibrium in relation to the mortality of normals from malaria.

and malaria the three types, *NN*, *NA* and *AA*, appear with the ratios expected from the simple Hardy-Weinberg proportions, whereas among the adults of the same populations there is a clear departure from these proportions of the kind that would be expected from the action of the two kinds of selection. The higher proportions of *NN* and *AA* individuals eliminated before breeding age just balance one another so that the proportions of the *N* and *A* genes remain constant in the population (Fig. 8).

If a negro population in which, because of its exposure to malaria, the sickle-cell gene is frequent is removed to an environment free from this type of malaria, the selective disadvantage of the *N* gene will be lost, though the disadvantage of the *A* gene, due to the production of the anaemic homozygotes (*AA*), will remain. In other words s_A will retain its value while s_N will be reduced to zero. Then from our equation (and see Fig. 7) the frequency of the *N* gene, u, must begin to rise and that of the *A* gene, v, to fall towards a new equilibrium where the *A* gene will be rare. The negro slaves taken from West Africa to North America underwent just this transformation of habitat. It is estimated from what is now known of West African tribes that the incidence of the sickle-cell trait in the original slave population must have been at least 22 per cent. Anthropological considerations suggest that during its time in the United States the negro population has been diluted by mating with whites and Indians to the extent that the frequency of the sickle-cell trait could have fallen to 15 per cent for this reason alone. In fact the incidence of the trait among United States negroes today is not higher than 9 per cent, that is about three-fifths of the 15 per cent expected if the fall had been due solely to mating with others than negroes. This difference is presumably due to the lessened disadvantage of the normal gene in the absence of malaria, and calculation shows that such a fall should take about 12 generations from the removal of malaria as a cause of mortality. The generations may well have been somewhat shorter in this negro population than in the present population of the United Kingdom, and if we consequently take it as 25 years, the necessary 12 generations would represent 300 years. Taken as an

average figure this fits sufficiently well with the history of slave importation into the New World.

Evidently, as indeed our consideration of the equilibrium would lead us to expect, the way to reduce the frequency of sickle-cell anaemia is to eliminate malignant tertian malaria, which in its turn means control of the mosquito which spreads this disease. So we have the curious situation that the invention

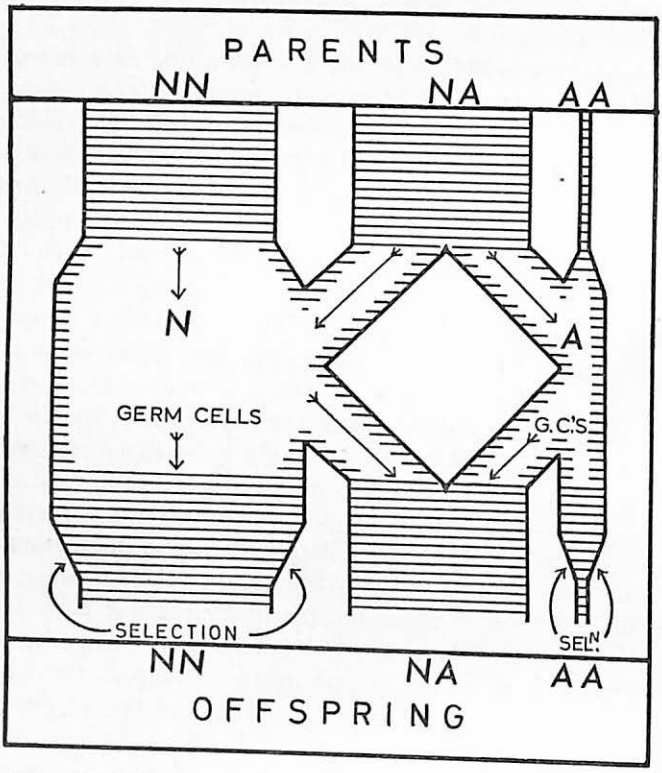

FIG. 8. Balance of selective forces in sickle-cell anaemia. The normals (*NN*) contribute to the pool of germ cells carrying the gene *N*, and the anaemics (*AA*) to the pool of germ cells carrying the gene *A*. The sicklers contribute equally to both pools. The germ cells combine at random to produce *NN*, *NA* and *AA* progeny in the Hardy-Weinberg proportions, the proportions of *AA* and *NN* individuals then being reduced by selection acting through anaemia in the case of *AA* and through malaria in the case of *NN*.

of that great killer of insects, D.D.T., may well have been a decisive event in combating the suffering from this biochemical upset of the haemoglobin. Treatment of the disease itself in so far as it was successful in lowering the disadvantage, s_A, of the sickle-cell gene would of course act in the other direction by raising the gene's incidence.

The balance of selective forces which governs the frequency of the sickle-cell gene is complicated in parts of West Africa by the occurrence of a further gene affecting the haemoglobin. This so-called haemoglobin-C gene interacts in its effects with the sickle-cell gene in such a way as to produce a variant of the sickle-cell disease in people obtaining the two genes one from each parent. The result is that while each gene appears to tend of itself to stay in a population for the reasons we have been considering, the two tend to be mutually exclusive, so that a high incidence of one is associated with a low incidence of the other. The distribution of the genes in West Africa agrees well with this expectation, and warns us of the dangers of using genes whose distributions are subject to such powerful and complex forces of natural selection in attempts to trace evidence of common ancestry among groups of peoples. Nor is this interaction of the sickle-cell and haemoglobin-C genes unique: similar situations almost surely hold with genes for other variant haemoglobins and for the disease known as thalassaemia in other parts of the world.

Polymorphisms in Man

Individuals displaying the sickle-cell character are both sharply distinct from the normals and moderately common in the population where they occur. Such a population is conveniently described as polymorphic, or as showing a polymorphism, for the character. The term is not applied where the character shows continuous variation, as stature does in all human populations, for the classes are not then sharply distinct from one another, nor where the variant is sharply distinct but rare as with achondroplasia. The sickle-cell polymorphism is but one example of many in man, though it is unusual in

that we know how the balance of selective forces works to bring it about. The haemoglobin-C character is another example of polymorphism which is probably maintained in a similar way. These polymorphisms are, however, confined to certain populations for obvious reasons. Others are as widespread as man himself. The most familiar is, of course, the polymorphism (or, if we wish to be very strict in our terminology, the dimorphism) for sex. Almost equally familiar now are the polymorphisms for the *ABO*, Rhesus and other blood group systems which are so important in relation to blood transfusion and, in the case of the Rhesus group, in relation to the occurrence of haemolytic disease in newly born infants.

All these blood group systems are under genetic control and in the case of the *ABO* and Rhesus systems the control is somewhat complex. Taking the *ABO* system first, it depends not on a pair of alternative genes but on a set of at least three, which are known respectively as the *A* gene, the *B* gene and the *O* gene. Any individual has two of these genes, obtaining one from each of his parents and passing on one to each of his children in the usual way, and the two genes may be alike or different. Thus he may be *AA*, *BB*, *OO*, *AB*, *AO* or *BO* in the genes he carries, but he cannot be *ABO* because the genes are alternatives, or alleles as geneticists would say, and short of a chromosome abnormality he can carry only two genes at this locus. The dominance relations of the genes are odd, because both *A* and *B* are dominant to *O*, but they are not dominant to each other. Thus while there are six possible genotypes, only four classes of individual are recognisable by the characteristic properties of their blood. These are the classes familiar to all who have been blood grouped for the purpose of blood transfusion or donation, viz. *O* (which includes only genetically *OO* individuals), *A* (which includes both the genetical classes *AA* and *AO*), *B* (which includes *BB* and *BO*) and *AB* (which again includes only genetical class *AB*). In general the *O* gene is commoner than either of the others with the *A* gene commoner than *B*. In the English population the frequencies of the three genes are about 70 per cent *O*, 25 per cent *A* and 5 per cent *B*. Now the Hardy-Weinberg rule applies in an extended form where there are three alternative

or allelic genes. If we write u, v and w for the frequencies of the *O*, *A* and *B* genes, respectively, with $u+v+w=1$, we expect the six genotypes in the proportions u^2 *OO*, $2uv$ *AO*, v^2 *AA*, $2uw$ *BO*, w^2 *BB* and $2vw$ *AB*, and in the absence of disturbance from selection or other agency these are in equilibrium. If we put the approximate English values of 0·70 for u, 0·25 for v and 0·05 for w, we expect then for

$$\left.\begin{aligned} OO,\ u^2 &= 0{\cdot}4900 \\ AO,\ 2uv &= 0{\cdot}3500 \\ AA,\ v^2 &= 0{\cdot}0625 \end{aligned}\right\} 0{\cdot}41$$

$$\left.\begin{aligned} BO,\ 2uw &= 0{\cdot}0700 \\ BB,\ v^2 &= 0{\cdot}0025 \end{aligned}\right\} 0{\cdot}07$$

$$AB,\ 2uw = 0{\cdot}0250$$

giving for the proportion of the four recognisable blood groups in the population

O–49 per cent; *A*–41 per cent; *B*–7 per cent and *AB* just under 3 per cent.

The frequencies, whether of genes or blood groups, are not, however, the same all over the world.[24] The *O* genes for example becomes less common and the *B* gene more common as we go eastward in Europe. Even inside the British Isles there are differences, with the *O* gene rising in frequency from a low value of about 0·67 in south-east England to 0·72 in Scotland and even as high as 0·74 in parts of Ireland. What determines the diversity in these blood genes, their frequencies within populations and the differences in their frequencies in different places?

The *ABO* is but one of the systems of blood groups which raise these questions. To take two more examples, the *MNS* and the Rhesus systems of blood groups each depend on a number of allelic genes which show diversity within virtually every human population that has been examined, and which vary in their frequencies from one part of the world to another. Nor are polymorphisms confined to blood characters. People fall into two classes according to their ability to taste the substance known as phenylthiocarbamide. The difference depends on a pair of allelic genes, usually denoted by *T* and *t*, that associated with inability or at least very low ability to taste the

substance being recessive to the other, so that "non-tasters" are *tt* while the "tasters" include both *TT* and *Tt* individuals. In Britain there are about three times as many tasters as non-tasters and while the proportions appear not to be quite the same from one population to another they do not vary so widely as the frequencies of the blood group genes. Nevertheless the tasting polymorphism raises just the same questions as the blood polymorphisms. How are we to understand this diversity?

Various interpretations have been attempted from time to time. Perhaps one of the most obvious is that the differences associated with polymorphism are to be regarded as neutral in their effects on fitness so that once established their frequencies in a population will not change, apart from chance vagaries. On this view the diversity within a population springs from its origin by mixture of different primitive groups or "races," the proportions of the present types reflecting the magnitudes of the original contributions from these founding groups, and the variation in polymorphic proportions arising from variation in these original contributions to the different populations. Such an interpretation runs into many difficulties. There are good theoretical reasons for doubting whether genes of any but the most trivial effect can be neutral in their effects on fitness. The blood group genes are certainly not trivial in their effects and, as we shall see in a moment, observational evidence is beginning to accumulate of their positive effect on fitness. Furthermore, if the present diversity is to be traced to ancestral mixture we should expect the polymorphisms for the different blood group systems to show some relation to one another in the proportions they display within populations and in the changes these proportions show from one population to another. There is little indication of such a relationship to be derived from the now extensive figures available for the common blood group systems throughout the world: the changes in proportions in each system cut right across the changes in proportion of the others. Implicit in this interpretation, too, is the idea that the diversity within present populations is derivative, arising solely from the mixing of the founding groups which were themselves pure each for one of the genetic components of each polymorphism. This merely

transfers the problem of accounting for the diversity, for it leaves unanswered the question of why the hypothetical groups differed one from another. In any case the *A*, *B* and *O* genes are known all to exist in the anthropoid apes while both tasters and non-tasters occur among chimpanzees. The genetical constituents of the polymorphisms must thus be older than man himself so that little advantage is to be gained by seeking to account for human polymorphisms in terms of human migration and mixing. True, mixing may affect the proportions of the genetic classes in populations and similarities in gene frequencies can stem from similarities in ancestry; but it can hardly be doubted that basically diversity is the common state for human populations, as for those of other species, even though the proportions in the classes may not be uniform. The "pure" race is a myth in man as it has been shown to be in other normally outbreeding species of animals and plants.

The sickle-cell polymorphism is maintained by the advantage which the heterozygote enjoys over both homozygotes, normal as well as sickle-cell anaemic, and it begins to move towards extinction when, as in the negroes of the United States, the advantage of the heterozygote over one homozygote is lost. If in the *ABO* system of blood groups the heterozygotes, of which there are more types than one, enjoy advantages over the corresponding homozygotes the polymorphism would be maintained here too, and the same is true of the other systems of blood groups. The tasting polymorphism is simple, depending on only two allelic genes, and would operate just like that for sickle-cell. Following a suggestion by Ford[14] a search has been made for associations between the blood groups and disease and it has become clear that such relationships do in fact exist.[25, 31] An association was first reported between blood group *A* and cancer of the stomach, to be followed by a further association between blood group *O* and peptic ulceration. The latter association proved to be complex, being stronger with stomal than with duodenal and gastric ulcers, and that with duodenal ulcers being in its turn stronger than the relation to gastric ulceration.[31] People with pernicious anaemia have also been shown to be more often of blood group *A* than would be expected purely by chance, and other possible associations

have been reported. Evidence implicating other blood group systems is also coming available.

It is thus clear that the blood group genes are not neutral in their effects on fitness: they do in fact affect predisposition to disease and the different genes affect this differently. We may therefore eventually track down the reason for the polymorphism in this way, just as has been done for the sickle-cell polymorphism; but we have not done so yet, for none of the relationships has provided an indication of that advantage which, on this interpretation of polymorphism, must be special to heterozygotes. True, in one case a special property of heterozygotes has been revealed, but it is a disadvantageous not an advantageous property and arises from the association of haemolytic disease of the new born with the Rhesus blood group genes.

There are many allelic genes in the Rhesus system but for our present consideration they may be grouped into two classes, those which may be termed Rhesus positive (Rh+) and the rest which are known as Rhesus negative (Rh—). The Rh+ genes are dominant to Rh—, in respect of this difference. Now where a Rhesus negative woman (Rh— Rh—) marries a Rhesus positive man (Rh+ Rh+ or Rh+ Rh—) at least half the children she conceives will be heterozygous (Rh+ Rh—) for the Rhesus genes, and since Rh+ is dominant to Rh— they will behave as Rhesus positives. While the child is still a foetus some of its red blood cells may get into the maternal circulation and such cells from a Rhesus positive foetus can stimulate the Rhesus negative mother to treat them as foreign organisms and manufacture antibodies against them. These antibodies in their turn can penetrate back from the mother's circulation to that of the foetus, or of any further foetus conceived subsequently, and attack its red cells if these are Rhesus positive. The result is haemolytic disease of the baby. A mother's early Rhesus positive babies seldom suffer because the production of antibodies is seldom stimulated to a dangerous extent during the first effective pregnancy, except where previous blood transfusion of the ordinary kind had resulted in the mother receiving Rhesus positive blood, so initiating the process. Any Rhesus negative babies the mother may bear

will also be free of the disease since the antibodies are specific in their attack to Rhesus positive red cells which such babies do not carry. Equally Rh+ Rh+ babies are not affected since an Rh− Rh− mother cannot produce them: all of her children must receive an Rh− gene from her. So the disease is confined to heterozygous babies (Rh+ Rh−). In so far as the disease results in a selective mortality of these babies it must eliminate the Rh+ and Rh− genes in equal numbers, and other things being equal this must obviously tend in general to eliminate the rarer of the two genes from the population. In other words, while heterozygous advantage maintains a polymorphism, heterozygous disadvantage destroys it. Yet human populations are polymorphic for the Rhesus character we have been describing. Either the polymorphism is the result of admixture—an explanation which we have seen to present its difficulties—or some other compensating factor still to be established is at work. Our information is not yet sufficient to provide the answer.

Heterozygous advantage will maintain a polymorphism but it is not the only agency which can do so, as we can see if we turn to the commonest polymorphism of all, that for sex. Women are homozygous (XX) and men heterozygous (XY) for the genes in which the X and Y chromosomes characteristically differ and which are responsible for the sex difference; but there can be no question of either sex being fitter than the other in the sense of contributing more to posterity, for every child must have both mother and father. Here the dimorphism is maintained because both sexes are essential, because by itself neither of them is fit in our sense of the term, reproduction depending on their simultaneous functioning in biological cooperation. Now wherever the relation between two or more types of individual is cooperative in this way, each being the fitter because the others are present, the polymorphism will be maintained, and although this cooperation is at its most obvious in reproduction it is not confined to this function, as we can see from studies of other species and as we shall see clearly in man when we come later to look at his social organisation. Where the maintenance of polymorphism depends on cooperation, the very diversity itself of the individuals is conferring

the advantage, not the special properties of one genetic class. Diversity in respect of the *ABO* blood groups may confer an advantage in that it limits effective migration of foetal cells into the maternal circulation and so reduces the incidence of haemolytic disease.[13] It is also possible that if the blood group systems are in any way related to resistance to infectious diseases, their diversity would help to limit the spread of such a disease to a proportion of the population. Different fractions of the population would be at greater risk from different diseases so while all would be at risk at some time, not all would be at risk at one time, the diversity thus securing continuity. This is, however, no more than speculation: we can list possibilities but we cannot in fact yet say with confidence how most of our polymorphisms are maintained.

Given that our polymorphisms are maintained by a combination or balance of selective advantages, any change in the selective forces that are operating must mean a prospective readjustment of the proportions of the types in the polymorphism, and this readjustment will proceed until a new equilibrium is reached. If the change in the selective forces is small the change in the proportions at equilibrium is likely to be small, and in any case the change may take many generations to complete, as we have seen in relation to sickle-cell in the negroes of the United States, where the equilibrium is still a long way from attainment even after a dozen generations, despite the gross alteration that abolition of exposure to malaria has brought about in the action of selection. With slow readjustment in response to change in the environment, the effects of race, migration and mixture may be a major and even dominant factor over long periods in determining the proportions of the types in a population. Indeed the United States negroes may well be regarded as revealing by their proportion of sickle-cell individuals, as large an effect of admixture with whites and Indians as of change in the incidence of exposure to malaria. Thus the frequencies of the various blood groups in the peoples of the world should reflect the great migrations and mixtures of the past, especially the recent past. But at the same time changes in the demands of the environment must be having their effects. A state of genetical diversity is normal in human

populations, as we have now come to see them. Furthermore, the frequencies of the different genetic types depend on the selective forces at work, with mutation also playing a significant part in certain cases. Therefore change in the conditions of life which affects the action of selection or the rate of mutation will inevitably alter the genetic balance and the frequencies of the different genes. These genetic effects of an environmental change may be slow to appear and it may well be that with many genes equilibrium is never attained because a further alteration supervenes in the environment before the genetic adjustment to the last has been fully achieved. This, however, serves only to emphasise the dynamic state in which, genetically speaking, human populations must be. Any change in the condition of life must have its consequences, trivial or serious, desirable or undesirable. Some of these consequences we are beginning to recognise, though as yet our knowledge is fragmentary and our understanding of the most imperfect.

6

Continuous Variation: Intelligence

Polymorphisms in respect of blood characters and tasting ability occur in all human populations. A number of the blood systems are complex in genetic determination, and if we take all the polymorphisms into account they divide each population up into a large number of genetically different types. Some of the types are common, but others are so rare that very few individuals fall into each of them, as we sometimes discover when an extensive search has to be made for a donor to provide the particular blood needed for urgent transfusion into one of these people. But, common or rare, these types are clearly distinct from each other: they are examples of discontinuous variation.

By far the greater part of the diversity that we find in all populations is, however, of the other kind, in which the spectrum of variation is continuous with the character in question exhibiting every shade of expression between wide limits. This continuous variation is obvious in respect of stature and bodily conformation, where even the most casual inspection shows each of us to be virtually unique. It is in fact shown by almost every character that a human being can display, physical, physiological and psychological, including that supremely important character, intelligence. It is, as we have seen, the variation in which Darwin was especially interested and it is indeed the variation which has in the main provided the raw material from which selection has wrought evolutionary change.

The same character will, of course, show both discontinuous differences and continuous variation. Achondroplasiac dwarfs for example are sharply distinct from their normal fellows in stature, but the normals differ amongst themselves by continuous variation. In the same way, sufferers from phenylketonuria are sharply separated from normals by their mental

deficiency, but the normals vary continuously among themselves in their intelligence. A few very short or very dull people arise merely as the extreme tail of the continuous distribution among normals and these may be confused with others whose abnormal dwarfism or mental deficiency springs from single gene differences such as those for achondroplasia and phenylketonuria. Generally, however, where the dwarf or the dull is the extreme expression of the continuous variation among normals, his parents and his sibs will be rather short or rather dull, whereas those whose abnormality traces to single gene differences will appear in families most of whose other members give no indication of any special tendency towards shortness or dullness.[30]

Differences contributing to continuous variation among the individuals may arise from environmental causes. Obviously, for example, nutrition must affect stature and bodily conformation and if individuals differ significantly in their nutritional status they must be expected to show differences in their growth and development. It has, however, been known since the time of Galton that continuous variation arises in part from genetical causes. Galton showed from his studies of stature in man that parents taller than average tend to have children taller than average and parents shorter than average to have children shorter than average. Similarly the children within a family tend to resemble one another in being taller or shorter than the average of the population. Now in the absence of an inherited effect we would not expect children to depart from the population average in the same direction as their parents. Thus in so far as the departure from average of the parents is due to inherited causes the children should depart in the same direction, and in so far as it is not the children should show no departure. The size of the children's departure from average relative to that of the parents, therefore, gives us a measure of the extent to which the differences in the population are due to genetic causes. It measures, in fact, what the animal and plant breeders call the "heritability" of the character, and so reveals the extent to which it is subject to alteration by change, fortuitous or deliberate, in the genetical situation.

Observations on stature in the British population show children in general to depart from the population average by just about half as much as do each of their parents. Since each child has two parents this suggests on the face of it that the whole of the variation in stature is due to genes. Such a conclusion must, however, be treated with caution for three reasons. First of all, spouses tend to be correlated in stature, that is tall men tend to have wives taller than average and short men shorter wives. So when we measure the children's departure in relation to the fathers' we are implicitly taking into account part of the mother's influence also and *vice versa.* If then we simply add together the apparent effects of the parents as we have just done, we overestimate the total genetic effect. A correction can be made in the calculation for this relation between spouses. Secondly, the observations available to us may well have been from a selected sample of the population and one which did not fully represent the range of nutritional and environmental differences. The result would be to underestimate the non-genetic effects and overestimate the genetic. This difficulty is probably much less serious now that the nutritional status of our population has approached a uniformly good level. Finally human parents give much more to their children than the genes. They provide the home and environment in which the children grow up. Thus even in respect of non-genetic agencies, members of a family must tend to resemble one another more than do individuals from different families. There is in fact a sort of inherited environment whose effects will become confounded with the effects of the genes passed on in normal inheritance. Again the result will be an over-estimate of the degree of genetic determination. In principles, these effects can be sorted out by observation on twins separated in early life and on foster children and adopted children, but at present the necessary observations are just not available. So we cannot yet assess the effects of the inherited environment. Nevertheless there can be little doubt that the continuous variation in stature is very largely, even if not wholly, traceable to differences in the genetic make-up of members of the population.

The story is much the same for intelligence—with one great

difference: stature is easy to define and measure, but intelligence is not. Difficulty in defining and measuring a character must induce caution in the assessment of our observations. It is, however, no reason for denying that conclusions can be drawn, and indeed within its clear limitations the use of I.Q. as a measure of intelligence allows valuable conclusions to be reached about the role of genetical determination of this character. There is a high correlation between sibs in respect of I.Q. and while, for technical reasons, the information about the relation of parent and offspring is more difficult to obtain, such as we have seems on the surface to suggest complete genetic determination of differences in I.Q. As with stature, however, there is markedly assortative mating, since people marry others in their own I.Q. range much more often than would take place at random. Also there must be a strong effect of the inherited environment on the expression of this character, so that the superficial appearance of completely genetic determination will be misleading. Observations on twins and foster children would seem to indicate that the variation in I.Q. is about three-quarters due to gene differences and one-quarter to other causes. Certainly it is highly unlikely that the genes are responsible for anything less than half the variation in I.Q. of our population.[19, 30]

Polygenic Systems

Galton's original demonstrations of the heritable component in continuous variation was made in man, but our understanding of how the genes work to produce continuous variation and how selection acts to change a continuously varying character is based almost entirely on breeding experiments with other species, among animals especially with fruit flies and mice. As we have seen, the basic postulate of the interpretation of continuous variation is that it depends not on single gene differences of large and specific effects, as do abnormalities like achondroplasia and phenylketonuria, but on the simultaneous actions of numbers of genes each of which has a small effect similar to and capable of supplementing those of the other member genes of the system. This interpretation has been

completely confirmed wherever it has been adequately tested, our evidence being especially full from experiments with the fruit fly, *Drosophila*. It is impossible for technical reasons to obtain anything but a minimal estimate of the number of genes comprised in a polygenic system of this kind, but we know that at least 18 genes must be involved in the best known case of variation in *Drosophila*. The number is almost surely larger than this and may be very much larger.

We can see how such a system works by considering an over-simplified example. Let us suppose that the variation in a character is determined by four pairs of allelic genes, *A–a*, *B–b*, *C–c* and *D–d*, the gene making for increased expression (for example, higher I.Q. or greater stature) being denoted by the capital letter in each case and its alternative making for reduced expression (for example, lower I.Q. or lesser stature) being denoted by the small letter. Let us further suppose that the effects of the genes are all equal and simply additive and that the members of each gene pair are equally frequent in a randomly breeding population. If we measure the degree of expression of the character in any individual by its departure from the average of the population, each increasing gene will add a unit to the expression in an individual carrying it, and each decreasing gene will subtract a unit. Then at one extreme an individual of constitution *AA BB CC DD* will depart from the average by 8 units in its expression, and at the other extreme an individual of constitution *aa bb cc dd* will depart equally in the opposite direction, i.e. by –8 units. Individuals of constitutions *Aa BB CC DD*, *AA Bb CC DD*, *AA BB Cc DD*, and *AA BB CC Dd* will be alike in showing an expression of 6, while at the other end *Aa bb cc dd*, *aa Bb cc dd* etc. will also resemble one another with an expression of –6. *Aa Bb CC DD*, *Aa BB Cc DD* etc. (there being 6 such types) will all have an expression of 4 as will also *aa BB CC DD*, *AA bb CC DD* etc. (there being 4 such types). There will of course be a corresponding set of types giving an expression of –4. Even more types will give expressions of 2 and –2, and most of all will give the average expression itself, denoted by 0 on our scale. The types themselves will not all be equally common in the population, *Aa BB CC DD*, for

example, will be twice as common as *AA BB CC DD* or *aa BB CC DD*; *Aa Bb CC DD* will be twice as common as *Aa BB CC DD* or *AA Bb CC DD* and so on. Then taking all these factors into account we expect the various expressions of the character to appear with the proportionate frequencies shown in Fig. 9.

The general resemblance of this distribution of frequencies produced by our model to that observed for stature or intelligence (Fig. 3) in man needs no stressing. The middle expressions are most common, the extreme expressions rare. True,

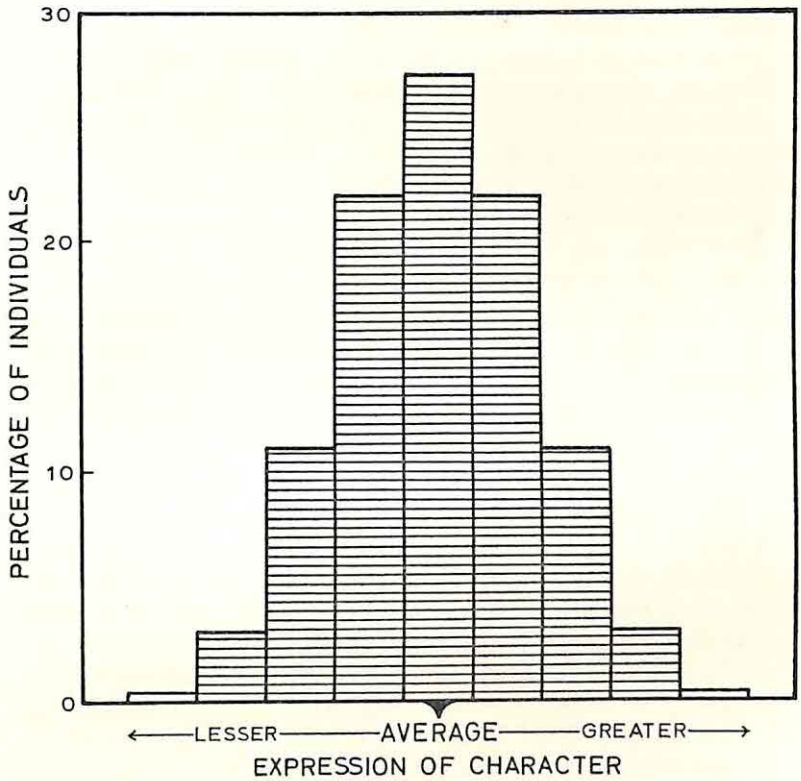

FIG. 9. The proportions of a population showing the various degrees of expression of a character under the control of additive genes at four loci, in the absence of dominance. Non-heritable variation has been neglected.

our model distribution gives only 9 grades of expression; but then it is an artificially over-simplified portrayal. With more genes, more grades of expression will appear, and if the genes do not all have exactly the same effect the grades will tend to blur into one another. Add some effects of non-heritable agencies and the blurring will increase to give a smooth continuity of expression. We have assumed the genes in our model to show no dominance and to be equally frequent in the population, neither of which assumptions need be true; but dominance and inequality of the gene frequencies do not alter the main features of the picture. Nor does a departure from random mating.

The essential feature of this interpretation is that the degree to which the character is expressed depends more on the numbers of increasing and decreasing genes the individual carries than on the particular genes present: the genes of similar direction are in this sense interchangeable in their effects, and the genes of opposite direction balance out irrespective of just which genes they may be. Thus to take a particular example in our model case, *AA BB cc dd* and *aa bb CC DD* have the same expression even though they owe it to diametrically opposed sets of genes. Further, this expression is 0, since *cc dd* balance out *AA BB* in the one case and *aa bb* balance out *CC DD* in the other. An individual of constitution *Aa Bb Cc Dd* will also have this same expression, the balancing now being between *A* and *a*, *B* and *b* and so on.

This balancing action gives rise to still another property of polygenic systems, that of hiding or storing variability. The idea of hidden variability is one that we have already met when considering recessive genes like that determining phenylketonuria. Only the *AA* homozygotes (to revert to the notation we were then using) displayed the character, the *NA* heterozygotes being normal in character. The *A* genes were hidden behind their *N* counterparts in such heterozygotes, yet the variation was potentially or prospectively present since the mating of two such *NA* individuals would give offspring of whom one-quarter were *AA*, displaying the abnormality and so revealing the genetic variation hitherto hidden. This same type of concealment is of course displayed by heterozygotes

for polygenic systems: two *Aa Bb Cc Dd* individuals mated together would give offspring of all the many types in the population including those with extreme expressions of the character, so revealing the variability hidden by the balancing effects of allelic genes on one another in the heterozygotes. But in polygenic systems this is by no means the end of the story, for as we have seen non-allelic genes can balance one another and therefore store variability in such a system. Thus *AA BB cc dd* and *aa bb CC DD* are alike in expression: they show no variation from one to the other. Yet if mated together, the second generation of their offspring could again reproduce every grade of expression of the character. The hidden variation has been freed by recombination (Fig. 10).

The fraction of its genetical variation that is concealed in a population by this balancing action of non-allelic genes will clearly depend on the number of genes in the system. With an effect dependent on only a single gene difference, like phenylketonuria, no variation can be concealed in this way, though of course some may be concealed in heterozygotes. With two genes of like effect, up to half of the variability of homozygotes, may be concealed by the balance of non-allelic genes. With three genes up to two-thirds may be concealed and with ten genes up to nine-tenths (Fig. 11). Thus the variability mediated by a polygenic system is like an iceberg: only a small fraction of it is displayed as differences observable between the individuals, by far the greater part lying hidden below the surface in the form of genic differences between individuals who, because of the way the genes balance out one another's effects, do not display the full effects of their genes (Fig. 13). So, great as may seem the continuous variation that we observe in stature or intelligence or other characters, it is no more than a token of the genetic variation that we actually carry in the population or of the changes and differences that would be produced if our genes were reassembled in different combinations by the action of selection. Our experience with other species suggests that an appropriate scheme of intensive selective breeding would take no more than a dozen or so generations to double or halve either the average stature or the average level of I.Q., according to the direction in which we applied the selection.

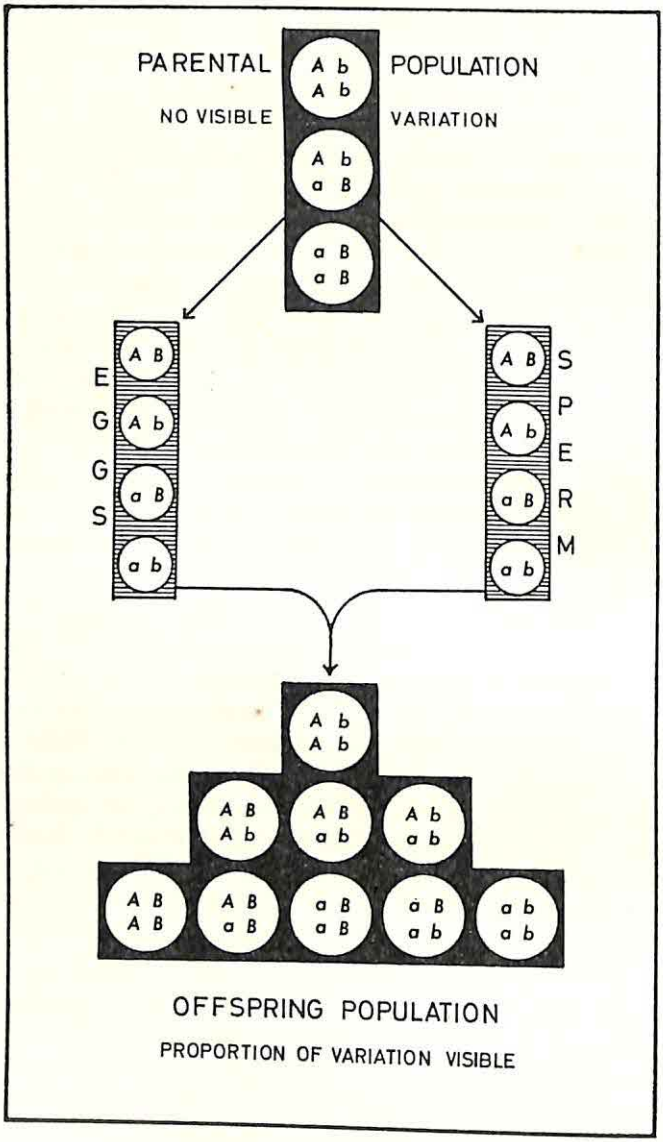
PARENTAL POPULATION
NO VISIBLE VARIATION
A b
A b
A b
a B
a B
a B
EGGS
SPERM
A B
A b
a B
a b
A b
A b
A B
A b
A B
a b
A b
a b
A B
A B
A B
a B
a B
a B
a B
a b
a b
a b
OFFSPRING POPULATION
PROPORTION OF VARIATION VISIBLE

FIG. 10

Now any force of selection, acting on a character, can distinguish between individuals only in so far as they differ in their expression of that character. If they do not so differ, selection will not discriminate between them even though they owe their expressions of the character to different genes. Thus in our model example, *AA BB cc dd*, *aa bb CC DD* and *Aa Bb Cc Dd* individuals show the same degree of expression. Thus selection could not distinguish between them, and the genic differences would be unaffected by the action of selection. Gene differences in fact are susceptible to selection only in so far as they display their effects in the individuals of the population: to the extent that the genic variation is concealed it is immune to the action of selection. The greater part of polygenic variation is concealed and so will not be eroded by selection. We must therefore expect a correspondingly large pool of it to build up. Observations on other species fully confirm this expectation. Like other gene differences, those in a polygenic system must have arisen originally by some process of mutation; but the amount of concealed variation that accumulates over the generations will be very many times greater than the increment added to it by new mutation in any single generation. We have a little evidence from experiments with *Drosophila* suggesting that, in respect of the number of hairs in a particular group on the fly, the pool of polygenic variation in a population may be as much as 1000 times as great as the amount added by mutation each generation. Thus the genes upon which continuous variation depends must in the main have been present in the population for very many generations, by

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FIG. 10. The release of hidden variability by recombination in the simple case of determination by two gene pairs of equal effect and no dominance. All three genetic types in the parental population have the same phenotype: all the variability is hidden by the balancing action of either alleles, in the heterozygotes, or non-allelic genes in the homozygotes. Recombination of the genes in the production of the germ cells, eggs and sperm, results however in individuals of nine genetic types appearing among the offspring. Not all the nine types of offspring have the same phenotype: some of the hidden variability has been freed by recombination.

contrast with, for example, the genes for achondroplasia 80 per cent of which have come into being by mutation within the preceding generation, and 80 per cent of which will be eliminated before the next generation.

Mutation is thus of very little significance for the continuance variation that a population shows, except on an evolutionary time scale. For the purposes of short term consideration we can neglect it. So while radiations, through their effect of raising mutation rates, can increase the frequency of abnormals owing their abnormality to specific gene changes

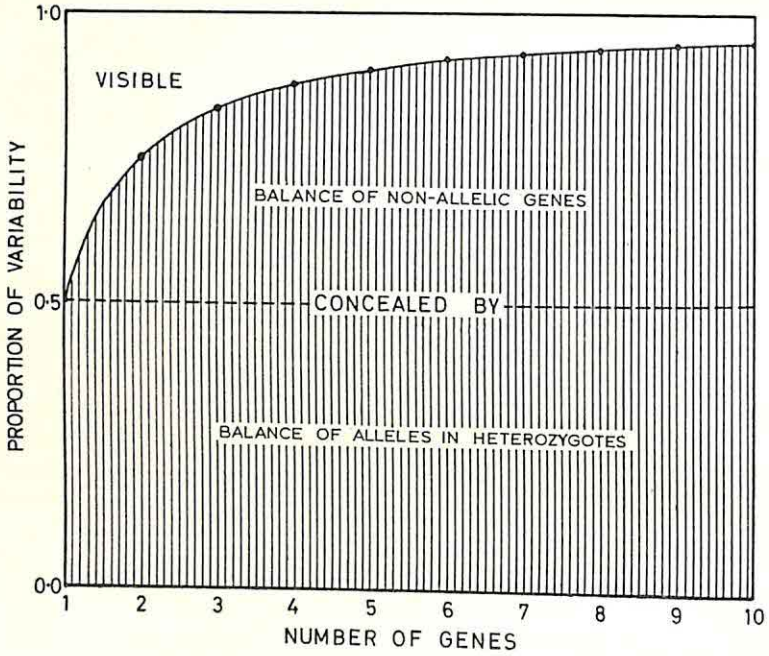

FIG. 11. The proportions of the variability which are, respectively, freely expressed and concealed in the genotype, in relation to the number of genes in the system. The genes are assumed to be of equal effect and all equally common in the population. The variation may be concealed by the balancing effects of allelic genes in heterozygotes or by the balancing effects of non-allelic genes in homozygotes. The proportion of the variation concealed by the balance of non-allelic genes rises with the number of genes in the system.

of the kind we discussed earlier, they will have only a negligible effect on the distributions of intelligence, stature and other characters among the normal members of the population who owe their differences to the action of polygenic systems.

The Action of Selection: Birth weight

Much of the genetic variability underlying continuous variation is concealed from the action of selection. Selection must nevertheless be supposed to be acting all the time on continuously varying characters, and its action is in fact clearly revealed by Karn and Penrose's observations on birth weight.[17] They record the birth weights of 7037 boy and 6693 girl babies born in a London obstetric hospital, between 1935 and 1946. The percentage of the babies falling in the different weight classes are shown in Fig. 12. The weights have been grouped into half-pound classes, that is those falling between 2 and 2½ lbs., 2½ and 3 lbs. etc. have been grouped together, for ease of representation and calculation. The boys were on the average heavier by a fifth of a pound than the girls, but they have not been separated in the figures as the behaviour of the sexes was fully consistent in all the respects in which we are interested. The distribution of the frequencies of the different weight classes among the babies is characteristic of a continuously varying character, the most common weights being those near the average with frequencies of occurrence falling off towards the extreme in the directions of both high and low weight. Penrose [26] has shown that just short of half of the variation in birth weight is traceable to genetic differences, some of them differences between the genetic constitutions of the mothers and some of them between the children. In so far as we can apply the simple concept of heritability to such a case we could say that the heritability of birth weight is about 40 per cent.

The hospital's records also supply information about the early survival of these babies. Taking the sexes together 614 or 4·47 per cent of all the babies were either stillborn or failed to survive the first four weeks after birth. The relation of mortality to birth weight is plotted for each weight class

between 3 and 11 lbs. in Fig. 12. Mortality is measured as the percentage of the babies in each weight class who failed to survive to four weeks and is represented on a logarithmic scale to avoid undue upward extension of the graph at the extremes. The picture is clear: the babies of near average weight have the best chance of survival, the mortality rate

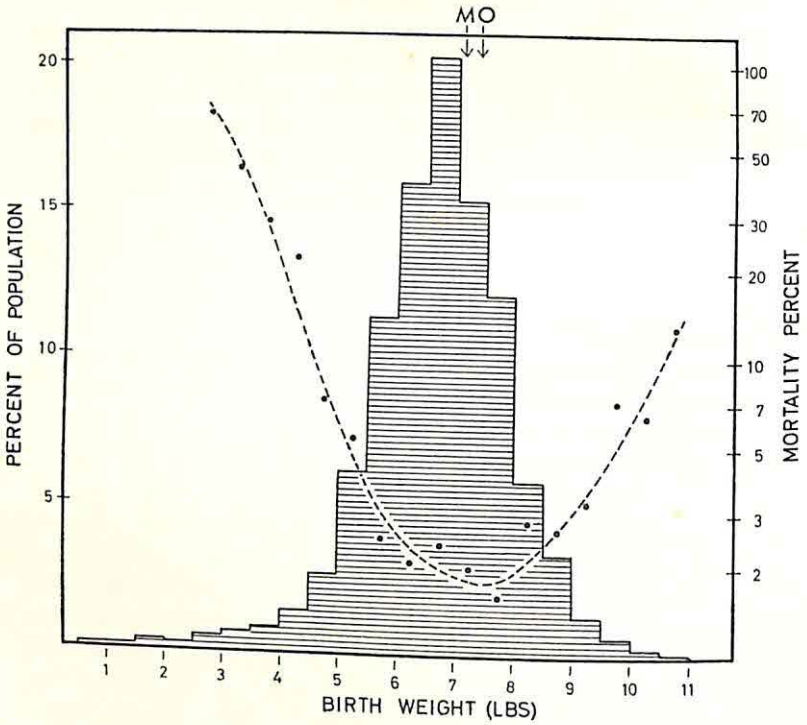

FIG. 12. The distribution of birth weight among 13,730 children and the rates of early mortality of the various birth weight classes. The hatched histogram shows the proportions of the population falling into the various classes in respect of birth weight. The broken line is the curve of mortality in relation to birth weight, the values actually observed for the classes of birth weight being represented by the points to which the curve is an approximation. The percentage mortality is set out as a logarithmic scale for ease of representation. *M* marks the mean birth weight and *O* the birth weight associated with the lowest mortality and hence to be regarded as the optimum weight. (Based on data from Karn and Penrose[17]).

rising sharply towards the extremes in both directions. Clearly natural selection is acting on birth weight and it is acting chiefly in such a way as to stabilise the expression of the character at or at least near its present average rather than to change it.

In so far as the variation in birth weight is due to genetic causes, such stabilising selection must be, generation to generation, tending to reduce the amount of variation round the average. Indeed in the present case the babies which survive show only 80 to 90 per cent of the variation (according to our method of measuring it) of the babies that were born. This is a great reduction and if we assume that it affects the genetic fraction of the variation as much as it does the non-heritable, a very few generations would see the heritable variation reduced to negligible proportions. Yet we have no reason to believe that variation in birth weight is in fact declining. Rather we must ask from where the reduction that selection is bringing about is being made good.

It may well be that this sample of babies is not characteristic of the population as a whole, and that the effect of selection in reducing variation is in fact less than this sample would suggest. Nevertheless, unless the sample is wholly misleading—and there is no justification whatsoever for so regarding it—natural selection must be acting to produce a marked reduction in the visible variation in each generation. This visible variation will, however, be itself but a fraction of the total genetic variability that the population is carrying. If there are ten genes in the system governing birth weight, the visible variation will be no more than some 5 per cent to 10 per cent of the total, the rest being concealed by the actions of both allelic and non-allelic genes in balancing out one another's effects in the way that we have already examined. If there are twenty genes in the system, the visible variation will be but $2\frac{1}{2}$ per cent to 5 per cent of the total and so on. So the loss of genetic variability from the erosion of stabilising selection is not in fact as great as it appears at first sight: it may well be only 1 per cent per generation, or even less, rather than 10 per cent to 20 per cent. This means that most of the loss in visible variation will be replaced in the next generation by recombination from the concealed store of variability (Fig. 13).

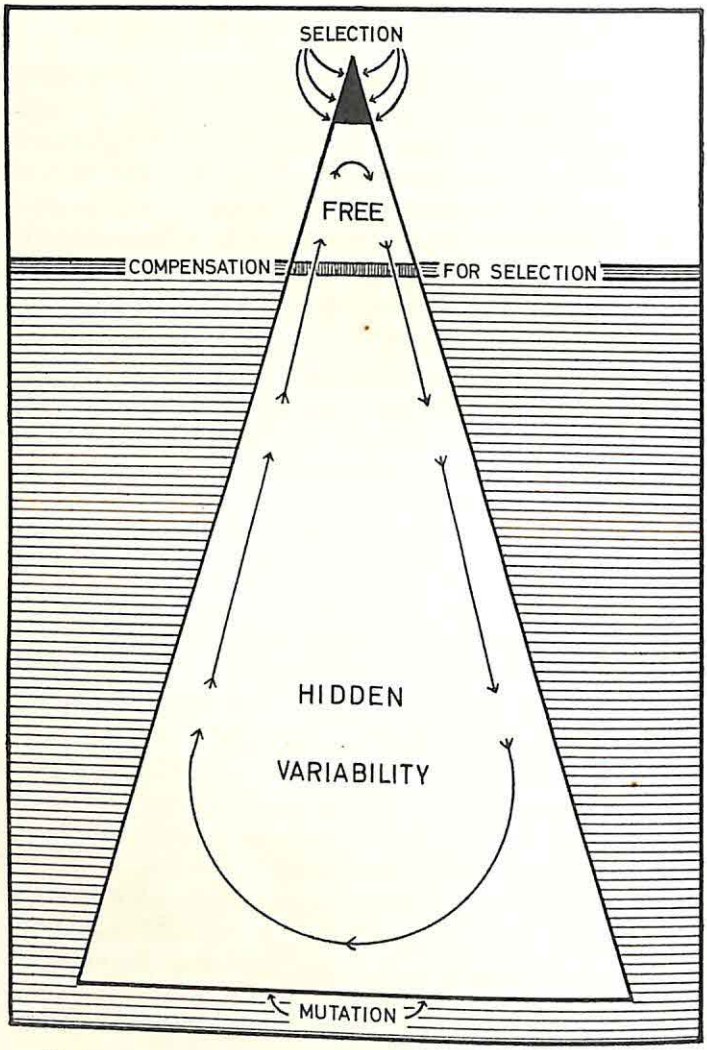

FIG. 13. Variability and selection in respect of birth weight. If ten genes of equal effect are assumed to determine the genetical component, only 5 per cent of the total variability will be detectable as actual differences in birth weight, the rest being hidden in the genotypes by the action of the genes in balancing out one another's effects. The selective action of differences in mortality removes ten per cent of the visible variation in each generation. This is compensated in the next generation by the release, through recombination, of hidden variability, the overall supply of variability being maintained over the long term by mutation.

As we have seen, balanced combinations of genes such as *Ab* and *aB* (to take the simplest example of two genes of equal effect) will have the same effect on the expression of the character; but they can, through the process of gene re-shuffling that goes on during sexual reproduction, give rise to the combinations *AB* and *ab* which differ markedly in their effects on the expression of the character (Fig. 10). If the *AB* and *ab* combinations have been penalised by natural selection in one generation they will be restored at least in large part by recombination of *Ab* and *aB* in the next. And the more genes there are in the system, the greater the opportunities for re-shuffling and recombination and the greater the fraction of the loss in visible variation that is restored by this means (see Fig. 11). Again we see the genetical picture presented by the variation visible in populations as reflecting the balance of two opposing effects, loss from selection and restoration by recombination. Again we see an apparently static situation as springing from a dynamic equilibrium: an equilibrium which, therefore, can be upset by any shift in the forces of selection that are at work or (though this is much more of academic interest) in the freedom with which genes recombine.

True, of course, unless selection is acting in a complex fashion, the restoration of visible variation by recombination from the store of concealed variability cannot of itself be quite complete, for the total variability has been diminished with the consequence that its redistribution by recombination cannot of itself reproduce the *status quo* completely. Mutation must be acting to make good any loss. Even the restoration of 1 per cent of the total variation by this means in one generation would imply a greater effect of mutation than has been revealed by observations on *Drosophila* already referred to. There the mutational increment was no more than 0·1 per cent or 0·2 per cent of the total, but in view of the uncertainty attaching to the various estimates and assumptions on which this comparison is based we should perhaps not attach too great an importance to the difference between the mutational increment observed for hair number in *Drosophila* and that estimated for birth weight in man: at least they are roughly of the same order of magnitude.

There is, also, always the possibility that the effective loss of variability resulting from the action of selection is less than it appears. Indeed there might theoretically be no effective loss at all. We saw in an earlier chapter that if, as with sickle-cell anaemia, selection acts in such a way as to favour the heterozygote at the expense of both homozygotes, both the alternative genes (*N* and *A* as we then termed them, or *A* and *a*, *B* and *b* etc. as we now are calling them) are held in the population with frequencies that are constant so long as the balance of selection remains the same. If, for the genes affecting birth weight, selection were to be penalising the homozygotes, there would be in each generation a reduction of variation by the differential mortality of the babies having the more extreme weights but without any reduction of variation in the next generation when it came to be born, for the variation would be restored by segregation from the heterozygotes which were being favoured by selection. This would imply, however, that the genes were having two distinct effects, one of them on birth weight and the other an unspecified influence on fitness, and that this effect on fitness did not arise directly from the effect on birth weight; or to put it another way that the very large or small babies did not have a higher mortality because they were very large or very small but because the genes that mediated their birth weights also happened to affect their fitness in an unspecified way. In respect of birth weight the heterozygote *Aa* might on this view, be intermediate in its effect between *AA* and *aa*, but in respect of fitness it would be better than either. Thus babies with average birth weights might be of a variety of genetic constitutions, for example *AA BB cc dd*, *AA bb cc DD*, *Aa Bb CC dd*, *Aa Bb Cc Dd* to revert to our four-gene model. Yet despite their similarities in birth weight the *Aa Bb Cc Dd* babies would have a better chance of survival than the *Aa Bb CC dd* etc., which in turn would have a better prospect than the full homozygotes like *AA BB cc dd*, *AA bb cc DD* etc.

This is clearly a possible view but one which, by divorcing fitness from birth weight, has evaded rather than answered the question of how natural selection is affecting birth weight itself. Furthermore, it is a view for which there is no evidence.

Intelligence

This discussion of birth weight in relation to fitness and selection would be of little more than academic interest if it did not bring out some of the difficulties encountered in seeking an understanding of how selection is affecting intelligence as measured by I.Q. The basic facts are generally agreed. Intelligence is a continuously varying character in the bulk of the population, showing a distribution similar to that of birth weight. The average I.Q. is 100 by definition, and a half or more of the variation appears to be genetic in origin. Now in various surveys that have been made the lower an individual's I.Q. the larger on the average the family (or sibship) from which that individual came. This would suggest that selection is acting against higher I.Q.'s, but the post-war survey of I.Q. among Scottish children shows no decline in I.Q. (in fact a slight rise) by comparison with a similar survey made nearly a generation earlier. Is there a risk of decline in intelligence as, it has been held, the relation of lower intelligence to larger families would imply, yet which seems to be contradicted by the surveys? Or is the relation with family size misleading and intelligence really stable? What in fact is happening to intelligence?

Let us look first at the way selection is acting. We have seen that babies of more extreme weight at birth, whether high or low, are at a disadvantage. The same appears to be true of other characters, including stature, in man as well as in a number of cases of continuously varying characters in other species. It is probably a general feature of such variation and there are theoretical reasons for expecting it to be so. Intelligence shows a similar relation[27], this time to fertility rather than survival, both fertility and survival being of course essential components of fitness. So there must be some stabilising action of selection on intelligence as on birth weight. Returning to birth weight, however, it can be seen from Fig. 12 that while the selection must chiefly be tending to stabilise the character by penalising the extremes of the distribution, the lowest mortality rate appears to be associated with a weight of about 8 lbs. as compared with an average birth weight of just over 7 lbs.

Selection appears thus to be tending to stabilise the character at a value slightly above the present average: there is some tendency to change the character, even if only to a very small extent. Though the selection is acting chiefly in a stabilising fashion, there is also a small directional element in it.

Thus even though both high and low levels of intelligence are associated with lowered fertility, so that there is a stabilising action of selection, there may also be a directional element in its action (Fig. 14). The increase in size of sibship as I.Q. falls has generally been taken as indicating such an action of selection in the direction of lowering the average intelligence. This negative correlation of I.Q. and sibship size holds good down to about I.Q. 70 or 75 below which level of I.Q. sibship size tends to fall again (Fig. 15). This suggests, on the face of things, that selection is favouring a fall from the present average of 100 towards this lower value. Two objections to this interpretation can be, and indeed have been, advanced. In the first place it has been argued that children from larger families score less well in I.Q. tests than others of similar intelligence from smaller families simply because in a larger family children receive less individual attention, live in more crowded conditions and so on. This is essentially an argument that I.Q. does not supply an adequate measure of inborn intelligence, that it is not enabling us to disentangle the genetic effects from the environmental. The interplay of genotype and family environment is a subject to which we must return later, when we shall see that it may be very difficult to separate genetic effects from those of very early environment and it would be hard to deny that family size of itself is completely without effect on the capacity to score in I.Q. tests. It is, however, equally difficult to accept this as the complete explanation for the relation as observed. The association of reduced fitness with many extreme expressions of a continuously varying character has been widely observed as well as theoretically expected, and intelligence shows clear indication of following the same pattern. In particular, lower intelligence is no longer associated consistently with larger sibships beyond a certain point. Rather the indications are that below this point, sibship

size falls with I.Q. (Fig. 15). The situation might well be held to be showing the picture expected from genetical considerations, with, however, the important feature that the largest families are associated with children not of mean I.Q. but of some 25 or 30 points below it.

The second objection is genetical. Penrose [27] has pointed out

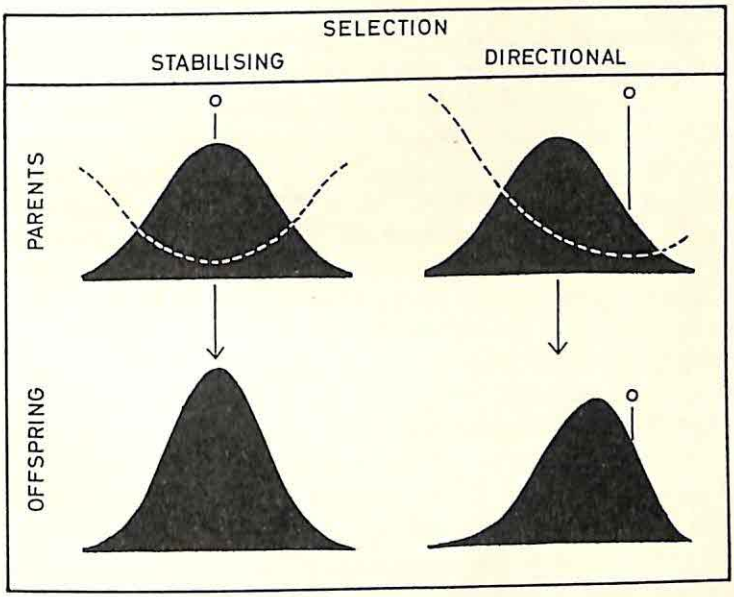

FIG. 14. Stabilising and directional selection. The solid figures represent the distribution of the character in the population and the broken curves the relative intensity of selection *against* the various expressions of the characters, *O* being the optimum expression in the sense of that suffering the least action of selection. In stabilising selection the optimum is at the average expression: the action of selection is to narrow the average of expression of the character. Birth weight (Fig. 12) is an example of such selection. In directional selection, the optimum is not at the average expression, and the selection tends to shift this average towards the optimum. I.Q. (Figs. 3 and 15) may be an example of such selection. Note that the curve in Fig. 15 is the reverse of that in this figure since (*a*) it shows the selection *for* I.Q. not that against it and (*b*) the optimum is *below* the average I.Q., not above it as in this figure.

that if individuals heterozygous for genes that mediate intelligence in a simply additive manner, are more fertile than their homozygous fellows, a relation can be obtained between I.Q. and sibship size similar to that observed while yet leading to a population stable in respect of its I.Q. distribution. There is no doubt that this could be the case, though whether this

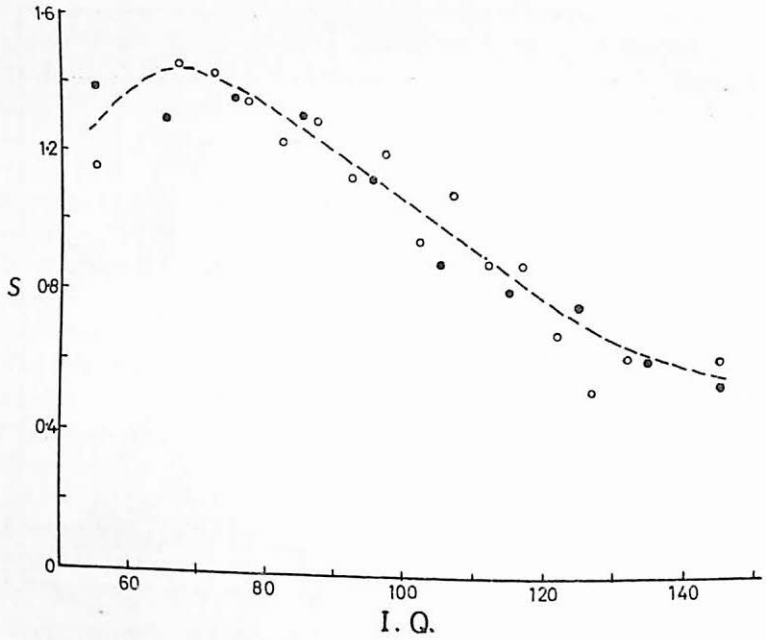

FIG. 15. The relation of size of family (*S*) from which children derive and the average I.Q. they show. (Adapted from Mather[20] by kind permission of the Royal Society).

provides a likely explanation of the facts as we have them is another matter. Some of the general difficulties raised by such a view have been looked at when we considered birth weight. There are specific difficulties, too, for Penrose's scheme provides of itself no explanation for the changed relation between I.Q. and sibship size below I.Q. 75, and it also demands that the genes tending towards lower I.Q. must in general be rarer than their alleles tending towards higher I.Q. This latter is a

postulate that cannot be disproved but the experimental studies of animal populations lend no support to it. Rather one would expect some of the genes tending to lower the expression of the character to be rarer and some to be commoner than their alleles.

On the whole, therefore, while the relation of I.Q. to sibship size is not incompatible with a stable situation in the population, genetical considerations would indeed point to the risk that forces of selection are tending to depress the average level of I.Q. Yet the Scottish surveys revealed no sign of a decline over several decades. If performance in the I.Q. tests was solely dependent on innate intelligence and quite independent of formal education, this would be a decisive finding. But can we be sure that children are not successfully trained to obtain higher scores in these tests? If they are, the stability or even slight rise in I.Q. as recorded from the tests could conceal a fall, albeit perhaps not a great one, in the innate intelligence that the tests seek to assess in the way that genetical considerations indicate to be, at any rate, a risk. At present we just cannot be sure of what is happening and we shall need a great deal more research before the situation becomes clear.

To take but one point, we do not know how adequate a measure of the fertility associated with a given level of I.Q. is provided in practice by the average size of sibship from which individual children of that I.Q. came. The two are obviously not the same thing, since individuals failing to leave children must obviously be taken into account in the assessment of fertility. Yet, at the same time they necessarily escape recognition in any calculations which start from children available for testing. In the situation which Penrose postulates, where heterozygotes have an advantage in fertility just because they are heterozygotes, size of sibship from which came the children of given I.Q. is no indication at all of the fertility of prospective parents having that same I.Q. But even in the absence of such heterozygous advantage the association of the largest sibships with children 25 to 30 points below the average may easily indicate that the greatest fertility is to be found in parents no more than 12 to 15 points below average. The pressure of selection may thus be much less than appears at first sight,

though it would still be towards depression of I.Q. More study is obviously needed.

We must be watching too for changes in the patterns of incidence of selection in relation to intelligence. It can hardly be doubted that this pattern has changed in the last hundred years and we must expect it still to be changing. Indeed there is evidence of such a change, at least in the U.S.A., where the decrease of family size with rising intelligence appears still to persist for I.Q.'s below 100, but where above this value family size rises with I.Q. as though the more intelligent parents are deliberately seeking to raise larger families.[15]

Any change in selection must have its effects on the genetical constitution of the population, since this is not static and rigid but, as we have seen, the reflection of a dynamic equilibrium between selection, recombination, and, to a lesser extent, mutation. If there is a direct relation between fertility and intelligence the impact of change in the selective forces is obvious. Even, however, if the relation is indirect, as Penrose has suggested, with intelligence and fertility affected by the same genes but in different ways, change in the forces of selection must still have its consequences. In such a case a fall in average intelligence is bound to follow from any change which reduces the disadvantage in fertility of individuals homozygous for the genes tending towards lower intelligence, in just the same way as the incidence of sickle-cell anaemia has fallen in American negroes because of the change in exposure to malaria.

Indeed, with a population in dynamic genetical equilibrium, any change in the incidence of selection will inevitably have its genetical consequences. We do not know how the genetical structure of our populations is changing, for we do not know how the forces of selection acting on it are changing. We can hardly doubt, however, that with alterations of family size, consequent on such things as family allowances, with improved medical services and with other forms of social welfare, the forces of selection are being altered. The adjustment of the genetical constitution of the population by deliberate intervention, as eugenists advocate, is generally regarded as something that we can choose either to undertake or to leave alone; but

in truth we must already be in the business of altering our genetical structure. What we are doing to it we cannot as yet see clearly. There are grounds for the fear that intelligence may be declining, though we cannot be sure whether this has been and still is so. Surely common prudence requires the truth of the situation to be established.

7

Social Transmission and Social Evolution

Intelligence, whose inheritance we have been discussing and whose importance we cannot doubt, is a difficult character to measure. It is essentially the ability to acquire, assess and use knowledge and for its measurement this ability must be distinguished from the knowledge acquired, assessed or used. At the same time, measurement of the ability requires that knowledge be offered for acquisition or be made available for assessment or use, so that in the practical field the distinction can never be made absolute nor the measurement unconditional. None of us comes to the intelligence test without knowledge, and indeed the test as we know it would be impossible if we did. Our performance will be in some measure dependent on this prior experience and the test can yield valid measurements and comparisons only in so far as this background is uniform and adequate for all under test. The older we grow the less easy it is to secure a satisfactory approximation to this condition: differences in intelligence may be so overlaid by differences in knowledge, which includes experience, as to become incapable of clear delimitation. And the greater the differences in the knowledge and experience gained in early life, the less reliable the comparisons that are yielded by tests at any age. The child of a savage society could be as intelligent as his fellow from an industrialised community and yet perform infinitely worse in intelligence tests as we know them. With tests designed to operate against a background such as would be normal in a savage society, the child of civilisation would be expected to do at least as poorly. With less contrasted backgrounds of knowledge and experience the advantages would be less sharp, but they may nevertheless persist, less obvious, more difficult to recognise or detect, and therefore more insidious

in their effects. Measurements of intelligence are clearly conditional, yet to recognise their limitations is in no sense to deny that within their limits (and their use in a society such as our own need not in general transgress those limits) they can yield comparisons which are both valid and valuable.

The distinction between intelligence and knowledge is clear in principle, albeit not always easy to apply in practice. It would be important even if each of us had to gain his own knowledge individually and without aid. It is all the more important in a human society where the knowledge and experience open to each of us for acquisition and use is the accumulation of countless other people, past and present, made available to us by a process of transmission which we may in the broadest sense term education. The ability to exploit and add to that accumulation is of paramount significance, and it has been made so by man's development of a new type of transmission, variation and evolution. All that has been said in earlier chapters about human diversity springing from the effects of the environment and from the action of genes could be presented as equally true for any species of animal or plant that is naturally outbreeding. The new type of transmission, variation and change, however, is unique to man and its effects, both obvious and subtle, are to be seen in man alone.

Man's special position arises from several capacities. He can learn from and utilise experience, and he can devise and use tools. In neither respect is he completely unique, though in both he is so much more highly developed than any of his fellow creatures as to be qualitatively different. Neither capacity could, however, have been exploited as it has, if it were not for the ability of individuals to communicate information and ideas one to another, to which has been added the further ability of recording information so that it can be stored in amounts beyond the capacity of the mind to carry, and in a form rendering it available to any who has acquired the necessary technique. Speech made communication possible immediately between individuals contemporary in time and coexistent in space. Repetition of the process allied to the ability to memorise made possible communication over time and space, to a limited degree. Writing removed the limitations imposed

by memory and the distortion consequent on repetition. Further developments have increased the size of audience we can address simultaneously, the amount of information we can store and transmit in manageable form, and the precision with which we can accumulate and present it. All these later developments were themselves, of course, made possible only by the utilisation of the initial ability to transmit information by speech.

There are thus at work in man two systems of transmission. One is the organic process of heredity which he shares with other species and which passes on the genetic determinants of biological development and behaviour. The other is the non-organic transmission of information and ideas between individuals who have no biological connection. Genetic transmission can be only from parent to offspring, and the "information" so transmitted can change and grow only as new combinations of genes, or ultimately only as new genes themselves, come into being. Social transmission on the other hand is not limited by biological relationship: in principle any individual can transmit to and receive from any other. It is a process resembling in its speed infection rather than heredity. Furthermore since the information transmitted is not dependent on the structure of biological molecules, like the hereditary materials, it is not limited in its rate of change and growth and in its complexity as the genetic information is. Social transmission therefore offers an immeasurably faster and immeasurably more flexible means of change than does heredity. Provided an individual can receive and act on instructions—or, as we might say, provided an individual can learn—his patterns of response and behaviour can be enormously more readily adjustable to the needs of the circumstances in which he finds himself than if he was dependent entirely on inborn reaction brought to him by the genes he received from his parents. Where the learning process takes place at a very early age its effects may not be easily distinguishable from those of the genes. Our attitudes to, for example, the use of violence or incestuous relationships are often regarded as inborn. Yet each of us is exposed from birth to the examples of our parents and others whose conduct and attitudes must surely colour our

own reactions to such practices. In fact few children display any basic distaste for violent action and even as adults we accept violence of an extreme form, for example in war, as a normal if distasteful reaction to at least certain situations in which we may find ourselves. In the same way there is sufficient evidence of incest both past and present for us to doubt whether an abhorrence of such practices came to us with our genes. The inborn and the early inculcated may indeed be hard to disentangle, more especially as our earliest training is so largely received from the very parents to whom we owe our genes.

Exosomatic Evolution

Organic evolution, to which all the immense variety of living creatures owe their origin, depends on the spread of favourable genetic changes under the impact of natural selection and it can move no more rapidly than differential rates of survival and reproduction allow. Its unit of time is the generation and its major changes must have required thousands or tens of thousands of these units. Man himself was brought into being by this same process of evolution and to it he owes not only his bodily form and physiological functioning, but also his special abilities, including the capacity for developing means of social transmission. These mental capabilities are genetically determined, display genetic variation and are subject to adjustment by selection in just the same way as other characters. They can have come into being by evolutionary processes no more rapidly than any of the anatomical and physiological features which distinguish man or any other species. Yet once in being they have enabled man to cast off the limitations imposed by the mechanisms on which the processes of evolution depend. He has been able to move into a new dimension of evolution in which the demands of the environment are no longer met and the limitations it imposes overcome by genetically determined adaptation of the individual himself, but by the accretion and construction of extra-corporeal devices which either fit the individual to the environment or in a wider sense adapt the environment to the needs of the individual.

Adaptation has ceased to be a property of the soma; it has become exosomatic.

The advantage of rapid locomotion that specially adapted limbs confer on other animals has been matched and outdone by machines such as the motor car into which man can insert himself when he wishes to travel and from which he can remove himself when his journey is completed. The power of flight which insects, bats and birds owe to their wings has been achieved by aircraft. The submarine and the aqua-lung have substituted for the gill. Glasses correct faulty vision and the television camera substitutes for the eye in otherwise inaccessible places. Radar does for man what their own special adaptations do for bats and electric fishes in warning them of objects and obstacles under circumstances where vision is of no avail. Clothes have replaced hair as an insulation against low temperature and in doing so have conferred a flexibility in adjustment to varying temperatures which a pelt of hair cannot match. Indeed since these devices are extra-corporeal they can be donned or doffed at will so that by their development man has achieved a versatility in meeting the demands of varying environments which would have been impossible by adjustment of the soma itself, and which is the most significant feature of man's adaptation to his environment.

Exosomatic evolution obviously requires the ability to use tools and to learn from observation and experience. It requires too the capacity for social transmission; for no individual could gain the knowledge, experience and skill for himself in his own lifetime to make possible such achievements. With the means of social communication each individual can draw on the accumulated experience of others, can transmit any addition he may be able to make to the accumulation, and can do so to a number of his fellows that is not limited by any special biological relationship. Indeed it is the means of social transmission that gives to exosomatic evolution both its scope and its speed. Furthermore, not only must each individual draw on others for gaining the knowledge, experience and skill that his own activities will demand, he also needs the actual assistance of others, whether of skills and training similar or complementary to his own. In other words exosomatic evolution

both requires and produces a social organisation founded on social transmission.

Social Organisation

Biology may be regarded as the study of organised entities, for the study of living creatures reveals to us systems of organisation at many different levels. The genetical materials themselves, the most fundamental materials of life, have a chemical organisation which endows them with the twin capacities of securing their own reproduction and of producing certain specific effects in the living cells that carry them. These materials consist of desoxyribonucleic acid (D.N.A.) which may be likened to a twisted rope ladder, whose two sides are composed of alternating phosphate and sugar radicles (P and S in Fig. 16). Each sugar has attached to it an organic base and these are joined together crosswise in pairs to form the rungs of the ladder. The bases are of four kinds, adenine (A), cytosine (C), guanine (G) and thymine (T), and they are always linked A with T and C with G. In reproducing itself the ladder, as it were, splits down the middle along the junctions of the base pairs so that each base no longer has a partner. A new chain of P and S and associated nucleotides then forms alongside each of the older halves, again with a new A matching an old T, a new T and old A and so on, so that two new complete ladders have arisen in place of the original one.

The genetical information which the D.N.A. carries and which by its own multiplication it passes on from cell to cell and through the germ cells from parent to offspring, depends on the sequence of the base pairs forming the rungs of the ladder. These may be four kinds, A–T, T–A, C–G and G–C and each rung may be of any of the four kinds. The varying sequence of these four along the ladder provides the basis for the genes, coding the genetic information rather like the way in which the varying sequence of dots and dashes conveys letters and words in the Morse Code. Crick *et al.*[9] have produced some evidence that a set of three successive base pairs is the meaningful unit of the genetic message, but much remains to be done before we can be sure of this.

The D.N.A. would, of course, be of little significance if it were not part of a further organised system, the cell, in which its message can be decoded and turned into effective action. The cell can be likened to a factory, in which the nucleus, comprising the genetic materials, constitutes the managing

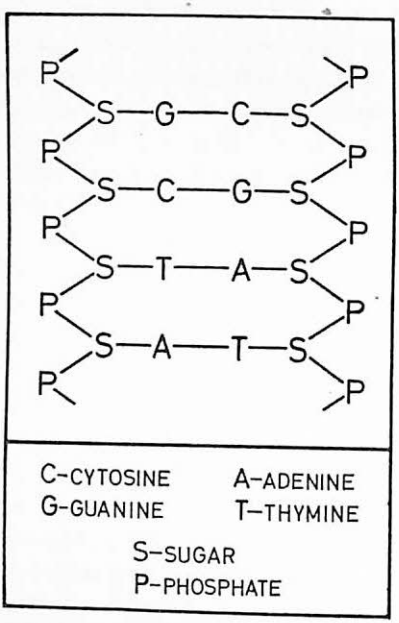

FIG. 16. The structure of D.N.A. The two chains consist of alternative phosphates and sugars, the sugars being linked between the chains by the pairs of bases. G is always cross-linked with C, and A with T, so that four kinds of linkage are possible as shown. Each linkage may be of any of the four kinds and the succession of the four kinds provides the ' code ' in which genetical information is carried.

office, and the rest of the cell—the cytoplasm—the factory floor where actual production goes on. The organisation of the cell is far from understood, but it certainly contains structures or organelles where its basic biochemical operations take place, rather as a factory has machines and assembly lines. These operate under the guidance of messages from the D.N.A.

It seems likely that ribosenucleic acid (R.N.A.), a chemical relative of D.N.A., conveys the messages and also gathers together in the cell the raw materials which are to be put together in the specific way dictated by the D.N.A. R.N.A. too, carries a code of bases which gives it the specificity it must have to carry out these tasks.

The cell is the unit of biochemical activity just as the D.N.A. is the unit of genetical information. In its turn, the cell is but part of an organised system at the next level of complexity, that of the individual body or soma. Every individual animal or plant consists of a number, generally a very great number, of cells which are alike in comprising a set of genetic materials and a cytoplasm, but which differ in the forms they take and the functions they discharge. We ourselves have many different types of cell—nerve cells, muscle cells, skin cells, liver cells, digestive cells and so on. Though some of their activities, for example the production of energy through cellular respiration, are common to all, the different types of cell discharge different functions. The well-being of the soma, and with it of course the well-being of every cell it carries, depends on these different types of cell, and the different tissues into which they are assembled, being present in the right proportions, at the right places and carrying out their right tasks in the right relations to one another. They are interdependent inside the system and if one type of cell or one tissue fails, all fail with it.

Even individuals, self-sufficient as they may be in respect of basic biological functions like breathing, feeding and locomotion, are but parts of a still further system in other respects. For example, in all but a few species of animals and in many species of plants, the individual is incapable of reproduction by itself. It needs a partner of a complementary type, of the opposite sex as we should say in respect of man and most animals, if reproduction is to be accomplished. For this function the individual is not a sufficient unit. Individuals in both animal and plant species are also bound by the evolutionary need for genetic diversity and by the need for diversity of form and character as a protection against predators, infectious disease and other special hazards of the environment.

In some species like bees and ants, a group of individuals is close knit into a community or society in which different individuals carry out specific and complementary tasks in relation to the life of the community, often taking on corresponding differences of form to do so. Here the individual is obviously but a differentiated part of the organised whole, just as the cell is but a differentiated part of the organised soma. Human societies are organised systems of individuals in just the same sense, though as we shall see, the agency which binds them together and controls them is quite different from that in the social insects.

In any organised system, whether at the level of genetic materials, cell, individual or population, the component parts must so develop that each discharges its own specialised function adequately and in such a way that it does not hamper the functioning of any other part of the system. This clearly involves a subordination of the part to the whole even at the expense of what would at its own level of organisation be a relatively advantageous development of that part. To take an example, all the cells in a soma arise by the division of pre-existing cells, but during the progress of development and the differentiation of tissues, most of the cells lose the capacity for continuing division. They do so in the interest of discharging their specialised functions of secretion, movement, nervous transmission and so on. Now any cell which fails to follow the proper course of differentiation and continues in division will have an advantage over its fellows in that it will contribute a greater proportion of the soma than will they. It will, at its own level of organisation, be a biologically successful cell, ousting and replacing its fellows. Yet in so far as by continuing in division it distorts balanced development and fails to discharge its proper specialised function, it harms the soma which is thereby put at a selective disadvantage. The success of the cell as an individual is purchased at the harm of the soma of which it is a part.

There is thus a conflict between the two levels of organisation cellular and somatic. At the one level success for the cell depends on aggression, at the other on co-operation. Clearly there must be some controlling agency at work, curbing the

aggression and ensuring the cooperation. This agency is the genotype, which governs the processes of the cell, its differentiation and its functioning as a specialised part of the soma. Furthermore, since the prospect of leaving posterity depends on the functioning of the individual as a whole, only those genotypes which determine adequately organised development will contribute to the genotypes of the next generation: natural selection will build up and maintain the genotype as the controlling agency of the individual's organisation.

The same is true at the supra-individual level of organisation. Males and females must be adjusted to one another morphologically and physiologically if reproduction is to be successful. The genotype ensures that they are so adjusted, and breakdown of balance in the genotype, as where the sex-chromosomes are anomalously distributed or where key genes have mutated, can lead to sexual upset and sterility. The other inter-relationships of individuals in populations of plants and animals are equally dependent on genetic control and adjustment. Even in the social insects this is still the case. In the bees and ants, the capacity for taking part in reproduction is confined to the queen and the short-lived drones. The workers are sterile, and in a sense are little more than detached organs of the queen, who will contribute her genes to later generations only in so far as those genes can bring about an adequately organised colony developing and working as a successful whole. Natural selection will settle with genotypes incapable of matching up to these requirements.

The genotype is thus the controlling agency at all levels of organisation and is even the link between individuals in populations of species other than man. It is so, because it is the essential element which links offspring with parent, and hence through the chains of relationship all individuals one with another. It is adjusted to this control by natural selection because its reproduction is organically tied to the reproduction of the individuals whose development and organisation it controls. Its success in control determines its own propagation.

With man, however, new factors enter in.

Human Societies

Genetically, as we have already had occasion to observe, man is like other out-breeding species of animals and plants. Like theirs too, his cellular processes, tissue differentiation and somatic organisation are under genetic control. Aspects of his supra-individual organisation like the relationships and mutual adjustments of the sexes are genetically determined as in other species. And in all these respects natural selection must have been responsible for the rise and maintenance of the controlling genotype.

Man, however, has developed a new system of social transmission between individuals and just like genetic transmission this offers the means of organisation of individuals into larger groups. And being both more rapid and more flexible in its operation it permits both speedier adjustment and greater complexity of relationship among the individuals of the population or society whose organisation it sustains. In these respects it stands in contrast to genetic transmission. Certain instructive comparisons may nevertheless be drawn. Genes are transmitted in heredity: ideas, using the term broadly to include beliefs, precepts, concepts, rules, laws and so on, are transmitted socially.

Just as the individual with the most effective set of genes will be successful in competition with other individuals, so the society with the most effective set of ideas—conventions, laws, precepts, canonical injunctions or however they may appear—will be successful in competition with other societies; for in so far as these ideas bind the society together into an effective and successful whole they secure their own perpetuation and even extension if the less successful society is absorbed into or learns from its more successful competitor. Success is here used in the Darwinian sense of securing perpetuation: it does not imply success in development of the arts or even technology except to the extent that these contribute to the perpetuation of the society as an organisation. It does not even of necessity imply military success, for although the perpetuation of a social organisation must frequently be facilitated by the successful use of force, a conquering society can become

absorbed into, and so obliterated by, the organisation and culture of the society which it defeats. The social structure, with the ideas from which it stems and by which it develops, is more important than the lines of descent of the people who compose the society: at this level of organisation the social bond of shared ideas becomes more significant than the biological bond of shared genes.

Ideas, like genes, are subject to the action of natural selection through the effects they produce. They are subject to variation, too, as genes are subject to mutation: even our most ancient and most deep-seated social ideas are constantly under challenge, sometimes by those whose actions we regard as retrograde and criminal, sometimes by those who we see as forward-looking and reforming, the distinction not always being easy to draw. With transmission, variation and selection, social organisation based on social transmission must be subject to adaptation and evolution just as is biological organisation based on genetic transmission. But just as social transmission differs from genetic in its properties, so does its variation and the way in which selection acts. Changes of ideas may be regressive in the sense that they lower the efficiency of social organisation, but they can be much more directly progressive and adaptive than mutations, whose effects in the organism are random and therefore vastly more often regressive than constructive. Selection too is not confined to competition between societies, or between groups and individuals within societies; it can take place between ideas in men's minds—a process for which there is no genetic counterpart as genes are prevented by the mechanism of heredity from competing one with another within the chromosomes and nucleus. Much of the selection in man's early days must have been between groups and societies, but as societies have become larger, fewer, and more powerful, competition between them, whether military or economic, has become prospectively so devastating in its outcome that a steadily growing premium has been placed on its avoidance and replacement by the weighing of ideas one against another. The difficulty is, of course, in the choice of criteria to be adopted in selecting among ideas, and if unlike criteria are adopted by different groups or societies these are always likely

to come into a competition in which the criterion of success is the ancient one of power, as is testified time and time again by the history of conflict both within and between societies.

Like genes at the biological levels, social ideas must determine both similarities and differences. If individuals are to work together cooperatively in a community they must be able to regard one another without a sense of menace in a number of basic respects. They must therefore subscribe to certain basic standards of conduct which the society must define and impose on all its members. If it fails to do so, it will be weakened and become more liable to fail in any competition that it may meet. Among the most ancient and most obviously necessary of these standards is the control of violence and especially the prohibition of murder. The level of violence to be regarded as permissible and the circumstances in which killing becomes murder are of course always subject to change and indeed have changed steadily. The prohibition of stealing is another obvious necessity, for if individuals must be constantly concerned about protecting their property from one another their cooperation must be weakened. But again, the point at which legitimate acquisition, whether by individual or community, degenerates into stealing is subject to divergence of views and therefore to change. All the individuals of a society must accept these and other similar though less striking principles. All must be alike in conforming and the community must establish its control both by making known to all its members the standards it expects (instilling them through upbringing and education) and by enforcing them with the use of whatever coercion is regarded as adequate and desirable.

These common standards are set by the social requirements of the community. They control the freedom of action of the individual, in order to establish the basis necessary for cooperation between the members of the community. The rules governing freedom of mating may also have a social significance in the same way, but unlike the prohibition of murder and stealing, they have an additional biological significance. All human societies have rules in one form or another against

incest, that is against inbreeding, and these rules are rigorously enforced. Now, as has been said earlier, man resembles any other outbreeding species of animal or plant in his genetical structure, and it is a feature of such species that inbreeding, that is the mating of close relatives, produces a progressive reduction in the vigour and fertility in the offspring—an inbreeding depression as it is called. As we have already seen there is evidence that man is no exception: the offspring of cousin matings have been found to display an increased incidence of general disease and disability [7] and there is some indication of a reduction in fertility too.[10] The closer, prohibited matings between for example parent and offspring or brother and sister, would be expected to result in greater and more rapid depression. Since the family is so important a unit in human cooperation, there would obviously be a risk of a high incidence of inbreeding if mating were uncontrolled: indeed the incidence would undoubtedly be higher than in species where close relatives separate and go their own ways at an early age. The rules against close inbreeding avoid this risk and in so doing help to maintain the biological quality of the members of whom the community is composed. By controlling the sexual relations between individuals they govern genetical quality. The selective value to the community is clear.

In primitive times, when these rules must have first become established, a group or community with an undue proportion of weaker and less fertile members would have been at a serious disadvantage in competition with its fellows. Other things being equal, the community would survive if its member individuals were biologically fit, and with the community would survive also the rules that promoted this fitness, just as the survival of a community with an adequate basis for cooperation would carry with it survival of the rules that provided that basis. Nor does it matter how those rules were held as having come into being, whether as divine revelations, as the precepts of legendary seers, as self-evident truths or in any other way. So long as they were accepted and enforced, biological fitness and social cooperation would be secured. Any belief or mechanism or even superstition that promoted their acceptance and enforcement would have its survival value, and by its

promotion of communal well-being would become accepted as an essential element in the social organisation.

Social transmission—education in its broad sense—is used to inculcate these standards, which all must accept. It must be used also, of course, to produce diversity because the essential of any organised system is the cooperation of unlikes, who because of the division of function which their unlikeness permits can jointly achieve more than would be made possible by the sum of their undifferentiated activities and uncoordinated efforts. The use of education for this purpose requires little comment: it is implicit in the training for the practice of the diverse crafts, professions and skills which are recognised as essential in a society. As the society grows and develops the variety of these special crafts grows too, and with the explosive development of societies under the impact of science during the past two hundred years, the need for corresponding diversity of training has grown equally. Indeed it is a gross oversimplification to discuss the organisation of human society at a single level. Each of us is a member of many different groups, the family, the craft or profession, the economic or other enterprise to whose activity we devote our labour and by which we earn our living, the social or recreational organisations to which we belong, the local community, the nation, the supra-national organisation. All of these make their demands, and not infrequently conflicting demands, on us. All require our cooperation, each in its own way, and all engage us in some forms of competition while requiring us to refrain from others. If the benefits of cooperation and of desirable competition are to be reaped and the ills from disruptive competition are to be avoided, the control must be correspondingly complex, and as the complexity of the system grows so must that of the control. In other words the task of education in fitting the individual to take his place in the society is becoming more complex. The rules he must know and obey grow in number and variety, but more important still the need for him to understand the principles which govern the relations of individual and society becomes increasingly urgent. In a changing society it is not sufficient for an individual to know the rules by rote. Only by grasping the basis on which society

is constructed can he adjust his behaviour to the needs of a situation which is always altering and always becoming more complex.

In the past much of the development of social structure has sprung from the conflict between societies and between groups within a society. Such selection is always wasteful of endeavour and may fail to achieve the desirable advance in social structure. With many simple societies, changing only slowly, the price was tolerable and the outcome at least statistically predictable. With fewer, more complex, rapidly changing and in no small measure interdependent societies the outcome is no longer predictable nor the waste and frustration tolerable. Conflicts of power between societies can indeed be catastrophic and conflicts within them can do little beyond demonstrating that any integral part of an organised system is essential to that system's well-being. Conflict of power must be replaced by conflict of argument, and as we have seen, this can succeed only in so far as the same standards are accepted by all for judging the merits and desirability of rival notions. This is a task for education conceived broadly and used wisely. Can we be confident that our notions of education are adequate to meet the need? Can we indeed be confident that our understanding of the society we live in is yet adequate to define the need? Research and experiment in social science and in education have become accepted; but they are inadequate in quantity and often ill-defined in direction. We must aim to understand the operation of cooperation and competition in all its aspects at all its levels of complexity, and to develop ways of educating the individual to play his part, not negatively and servilely but actively and constructively, in a society which operates not only for its own benefit but for that of all its members.

Of one thing we can be sure. Our society will continue to change and evolve as knowledge grows and circumstances alter. Many cherished notions will go. New restrictions will be imposed and old ones reviewed. Our notions of right and wrong will alter: indeed they are altering all the time, the changes sometimes being accepted quietly, at other times lamented loudly. Such alterations are essential because they reflect the changing needs of control in the evolving society. We must

always test such alteration in respect of both need and adequacy; but given need and adequacy, we should not oppose a change just because it is a change, because it is restrictive or because it may not suit our narrow sectarian interest. One of the great aims of education should be to teach us how to test, assess and, when need is established, accept.

8

The Interplay of Genetical Differences and Social Development

Two systems of transmission, control and change exist side by side in man. At the biological levels control is by the genes, which are transmitted in heredity from parent to offspring, adjustment being achieved and maintained by the action of selection on genetic variation. At the level of social organisation, however, control, change and development depend on social transmission which in its turn rests on man's ability to communicate, to learn and to generate ideas. These capacities are themselves a genetical endowment: lacking certain of the normal genes, man is virtually incapable of displaying them at all, and the complexity of the ideas which he can communicate, learn or generate is conditioned by his intelligence which, as we have seen, is in major part a reflection of his genotype. Thus, while social transmission has lifted organisation and development in human society beyond the limitations of genetic adjustment, it is itself dependent on genetic adjustment. The two systems have their inter-relations and we must expect them to interact in their expressions and effects. Indeed we have already seen one example of their interaction in the use of social means to control the mating system so as to avoid close inbreeding with its unfortunate genetical consequences.

A low level of exosomatic evolution and social organisation may clearly result from either of two shortcomings. It may reflect a failure to achieve the genetical adjustment necessary for the full expression of social transmission and social development. The mentally retarded do indeed fail to fit into society as we have developed it and a community of them would obviously be incapable of social evolution. Nor would such an inability be confined to those suffering from gross mental

retardation: the capacity for social evolution of a community of mentally dull individuals would be extremely limited. Equally, however, a low level of social development may do no more than reflect the failure of a people to exploit as fully as others have done a perfectly adequate genetic capacity. Many non-European peoples, especially savages, have been regarded as genetically inferior because their level of social development was below that of the European, and this view has drawn strength from these people's obvious genetical departures from the European in colour and physical characteristics. The existence of one genetical difference makes it easier to impute another. The falsity of such an argument is self-evident. Since genes can recombine, their effects can be re-associated, so that differences in the genetic determinants of one character do not imply differences in the determinants of another. In truth we know little or nothing about the comparative levels of intelligence of the world's peoples and the intelligence tests that we use, with success, to obtain comparative ratings within a population such as our own can do little to help us where the early background of training and conditioning within the family differs as widely as it does from one people to another. Of one thing we can be sure: there will be wide variation of the inborn level of intelligence among the individuals of all populations and peoples, and the ranges of intelligence from different peoples will show wide overlap. Beyond this, however, we can hardly go. We have no more justification for saying that there will be large differences in the mean levels of different peoples than we have for asserting that there will be no differences whatsoever in these means. By comparison with other characters and other species, one might expect differences to exist between the mean levels of inborn intelligence of different peoples but differences small by comparison with the variation within each population. To say this, however, is no more than to express an opinion: reliable evidence has yet to be obtained.

The difficulties of separating genetically and environmentally determined differences are familiar to all geneticists concerned with metrical or continuous variation. The difficulties of distinguishing genetical and social differences, of separating

the inborn from the early inculcated, are at least as great. Occasionally the distinction is made clear, as for example by the Black Caribs of British Honduras who though of negro ancestry display a Carib culture which they have acquired since their forced migration across the Atlantic in the days of the slave trade.[12] Jewish communities show us the same thing. Though related in ancestry more nearly to one another than to the peoples in contact with whom they live, they differ from one another in ways which reflect something of the differences between the societies of which they form part. Even so, despite wide separation and despite wide differences between the societies to which they attach, Jewish communities still retain common social features which are recognised as Jewish, including their religious practices. This in its turn emphasises a further point. Social characteristics may be transmitted as faithfully as, in some ways even more faithfully than, genetic.

The faithfulness of social transmission is exemplified by any society with a class structure of the kind which in the past has been such a feature of our own. Despite overlap, differences in socially transmitted characteristic modes of conduct, speech, dress, and even mental attitudes and modes of thought are clear between classes, by contrast with the absence of any sharp genetical differences. Hereditary skills which may be a feature of families or particular sections of the community have been held to spring from genetical differences and indeed it is impossible to demonstrate that genes never contribute to them. They must, however, rest chiefly on the social transmission of attitude, interest and know-how from parent to offspring or at least from one individual to another within the family or within the circle. Again we are brought up against the problem of disentangling the genetic and social contributions that parents make to their children's attitudes and educability. Shields[32] has shown that identical twins brought up apart are nearly as alike as twins reared together, not only in physical characters but in intelligence and personality too: the genetic seems very much to outweigh the social in its power of determination. But can we doubt that even if intelligence is essentially genetic in its determination, the preparedness to use it, the use to which it will be put, and the acceptance of education

to develop its prospective use are affected profoundly by the attitude of parents and the immediate circle, that is by social as opposed to genetic transmission?

Parents must certainly effect their children's education and educability by their social transmission as well as by the genes they pass on. And why should we be concerned that this is the case? Why should we be prepared to accept (as we do, albeit sometimes reluctantly) differences due to the genes children receive from their parents, but deny as unfair (as is so often done) even the good influence of parents on their children's education and educability where these are socially transmitted? The need is surely for recognising the effects of bad social transmission as distinct from poor genotype so that appropriate educational measures can be brought into use to upgrade the individual. Social attitudes to formal education do indeed change, and are at this very time changing radically. The pressure on places in institutes of higher education, especially the universities, reflects not at all an alteration in the genetic constitution of the population and only in part even the increase in birth-rate of the early post-war years. To a great extent it springs from a rapidly widening desire of parents to see their children receiving such an education—though whether this sometimes reflects a desire for the status of having a child at the university as distinct from a belief in the fundamental benefits of higher education is another and more difficult question to answer.

Both the genetic and the social endowments a child receives are variable, with the difference that the former is at present uncontrollably so while the latter is controllable. The need is to adjust the controlled to the uncontrollable. It is useless to give a genetically less gifted individual the education for a learned profession: he will be unable to absorb and utilise it and it may well deny him the possibility of an education from which he could profit and by virtue of which he could come to make his own special contribution to society. Equally it is a clear waste of material, from society's point of view, if the genetically gifted individual is not educated up to his ability. Full effectiveness can be achieved only by joint genetical and educational quality; by marrying genetical and social transmission.

In seeking high quality we used to place emphasis more on early conditioning, which we have seen may run more uniformly in families than do genes. The emphasis was on the family background. Now we recognise genetical differences and place emphasis on genetical quality which we try to pick out no matter in what family it may appear. This in its turn poses its problems, and problems not merely of the means by which inborn ability is to be recognised. It is a commonplace that true education comprises more than a specialised knowledge of some discipline of learning or even a technical understanding and balanced judgment of the field. It implies also an interest in the whole range of human endeavour and achievement; an informed interest in the affairs of the community and an understanding of the significance for the community of one's own specialised learning and ability; an appreciation of standards of value beyond those that are professionally one's own; and an intellectual toleration of all but the superficial and the shabby. Much of the necessary attitude has in the past stemmed from family transmission, but if in the future we cannot count on this to the same extent among, for example, students, our universities and indeed other places of education must be re-moulded to meet the new need. Some universities and other institutes of higher education are even now endeavouring to do this, but only experience can show the extent to which they are achieving success.

Social Change and Genetic Change

Social transmission can be used to level out inborn differences among men as when all are taught to conform to the requirements of society. It can also magnify the effects of the genetically unusual individual. The achievements of the great religious leaders or the great scientists, to take but two examples, were possible only to men of unusual inborn qualities; but they could be spread by social transmission to all men capable of comprehending them and so extended and developed for the benefit of all. Education in the broadest sense should be designed to exploit the effects of high quality genotypes and so to promote social advance in all its aspects, and not merely its

technical development. Such social advance is achieved by utilising what is genetically available and neither implies nor depends on genetical change. Recognition of the difference between genetical and social causation of difference and change is thus vital. Since social advance can be achieved without genetic change there is little argument for major interference aimed at raising the broad genetical level of intelligence, though of course the elimination of genetically determined physical and mental suffering is obviously desirable.

Social and exosomatic evolution does not imply genetic evolution and indeed it could even conceal genetic decline. Provided that at least some individuals have the genetic quality to be innovators and the body of the population have sufficient inborn capacity to learn from them, society can progress. This obviously requires a certain level of genetic capacity in the population, below which a fall would result in social stagnation and eventual decline; but at least until this point is reached the genetical quality of a population could decline behind a facade of continuing, even if decelerating, social progress. Nor in modern society have we any built-in safeguard against such a development.

All levels of biological organisation, other than that of society as we have been describing it, are under the control of the genotype. Reproductive fitness depends on adjustment at all levels, with the consequence that natural selection will keep all adjusted by its action on the genotype. In man, however, there are two kinds of transmission and two kinds of reproduction, biological and intellectual or social. These two forms of reproduction need not, and in fact do not, go hand in hand. The teacher's intellectual children are other people's biological offspring, and neither his satisfaction in intellectual reproduction nor the success of the society to which he belongs and which he serves depends on him having a large biological family too. The genetic quality required for intellectual reproduction does not imply the genetic quality for reproductive fitness in the biological sense.

Such cannot always have been the case. In earlier days when the family was a much more self-sufficient unit in the community (which at first could have consisted of little more than a

large family unit) failure in competition with other such units could have stemmed from a rate of biological reproduction too low to maintain numbers or from a level of intelligence too low to maintain within the unit an inventiveness, learning and transmission sufficient to cope with competitors. Adequate fertility and adequate intelligence were both essential, indeed since biological reproduction requires not only the production of offspring but providing and caring for them through their early years, intelligence and effective social transmission were important components of biological fitness itself. In such a society genetical and social transmission would be locked together, with the fitness of the group depending simultaneously on both and with both genotype and social structure under adjustment by the same forces of inter-group selection.

In modern society this is no longer the case, for the family has ceased to be the unit for most of its activities. In particular, though the welfare—physical, economic and educational—of an individual still depends in some measure, especially in the early years of life, on his family, it is becoming increasingly the concern of the community as a whole. In the social sense, therefore, the welfare of the individual is becoming increasingly dependent on the properties of the society rather than on those of the family to which he belongs, so that the genetical quality of the society is becoming of more importance than the genetical quality of the individual's own relatives. Within the society therefore the genetically less well endowed may be enabled to survive and multiply more rapidly and effectively by the activities of the genetically better endowed, who under a simpler system would be their competitors. Social activity has changed the balance of the internal forces of selection with the result that genetical quality and family fitness have become prospectively divorced.

We have seen in Chapter 6 that surveys have revealed a negative correlation between I.Q. and size of sibship. There is thus a case for the fear that the average level of intelligence may have been declining, though, as we have also seen, the evidence is in some respects contradictory and by no means conclusive. There is some indication too that at least in certain western countries the negative correlation has changed, so that

if decline there were, it may have ceased. Nevertheless with society as a whole taking responsibility more and more for the welfare of its individual members, the pressure of selective forces must be changing and genetic decline behind a facade of social advance is a possibility clearly to be reckoned with. Our knowledge of genetical variation in man and of the selective forces that impinge on it, is too slight for us even to be fully sure about the significance of the negative correlations that we have observed. Now intelligence is the most important character that man possesses. It is the character which has made social transmission and social evolution possible: the character which has allowed man to cut free from the limitations of genetic transmission and biological change. It is imperative that we should ascertain how the genes act and combine in its determination, how the forces of selection impinge on it and how it is changing—if it is changing—as the development of society alters these forces. We should aim to obtain the knowledge to recognise genetic dangers and to overcome them before the, fortunately slow, progress of genetic change has gone far.

To circumvent genetic risks, where these are shown to exist, may involve interference with the mode of life of the individual, with the individual's "rights," by imposing new "duties" on him. This, however, would merely reflect the way in which all organisation, whether biological or social, is developed and refined. The individual's freedom is necessarily restricted and duties are imposed on him in any society: no society can enjoy the fruits of social advance, for example in scientific, industrial, medical and welfare developments, while its members deny social organisation by standing on their rights as individuals in other but cognate connections. This principle is of course generally accepted in everyday life, or we should object to traffic regulation, the control of industrial practices and restrictions on the use of fire, dangerous chemicals or ionising radiations which could if handled carelessly harm others besides ourselves. We must recognise that the same principle must apply to genetical hazards, for the genes we possess, individually and as a population, are our basic heritage upon which in the long run all else is built. Education in the broadest sense, or conditioning if the term is preferred, is the

means by which the individual is fitted into society, and the scope of education or conditioning must be broadened as the growing complexity of society and its activities makes greater demands as well as confers greater benefits on its individual members. So we return again to the need for developing our knowledge of sociology and education in the fullest sense. And this must include an appreciation of genetical diversity and its significance for society: sociology is an understanding of society built on biology even though transcending the immediately biological.

Geneticists recognise that genes interact and sociologists that social influences interact. They must come together in the recognition that the genetic and the social interact in ways that are fundamental to each other. Already they have the common principles of transmission, variation and selection, to use the biologist's terms for them. These principles manifest in different ways, depending on different mechanisms at different levels. Our need is to explore them in their applications and interactions at all levels. Society is the end product of biological development; it is composed of biological entities and its structure rests on biological properties. The study of society must play its part in the greater biology.

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Index

HUMAN DIVERSITY

the nature and significance of differences among men

Kenneth Mather

What makes human beings different from one another? Why is it that each of us is unique? Human diversity has been the subject of interest and speculation since the beginning of man. It has been accepted as inevitable and bewailed as unjust; made the basis of reverence and of persecution; attributed to divine creation and to diabolical intervention. It has been traced to heredity and to the environment, to ancestry and to upbringing, often with a gross distortion of the evidence and a perverse interpretation of the conclusions.

In this fascinating study Kenneth Mather sets out to look at the various causes of diversity—environmental, genetical and social; to see how they act and interact; and to examine the way natural selection is related to and works on the differences they bring about. The reasons for our differences in blood groups are discussed; the causation of metrical variation in such characters as stature, birth-weight and intelligence is set out and the action of natural selection in stabilising birth-weight is analysed. The author then considers the question of whether selection is acting to lower the average intelligence. The book is not addressed specially to the professional biologist (though it is hoped that biologists will find some interest in it) but rather to all those who seek a better understanding of human differences and their importance for our populations and societies.

Kenneth Mather, now Vice-Chancellor, University of Southampton, was formerly Professor of Genetics in the University of Birmingham. His other publications include *The Elements of Genetics*, *Biometrical Genetics* and *Genes, Plants and People*.

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